



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : C12N 15/12, 5/10, 1/21, C07K 14/47, 16/18, C12Q 1/68, G01N 33/50, 33/53, 33/68, A61K 38/17		A3	(11) International Publication Number: <b>WO 98/39446</b>  (43) International Publication Date: 11 September 1998 (11.09.98)																												
(21) International Application Number: PCT/US98/04482  (22) International Filing Date: 6 March 1998 (06.03.98)  (30) Priority Data: <table border="0"> <tr><td>60/040,162</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/040,333</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/038,621</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/040,161</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/040,626</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/040,334</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/040,336</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/040,163</td><td>7 March 1997 (07.03.97)</td><td>US</td></tr> <tr><td>60/043,580</td><td>11 April 1997 (11.04.97)</td><td>US</td></tr> <tr><td>60/043,568</td><td>11 April 1997 (11.04.97)</td><td>US</td></tr> </table> (Continued on the following page) (71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). FISCHER, Carrie, L. [US/US]; 5810 Hall Street, Burke, VA 22015 (US). SOPPET, Daniel, R. [US/US]; 15050 Stillfield Place, Centreville, VA 22020 (US). CARTER, Kenneth, C. [US/US]; 11601 Brandy Hall Lane, North Potomac, MD 20878 (US). BEDNARIK, Daniel, P. [US/US]; 8822 Blue Sea Drive, Columbia, MD 21046 (US). ENDRESS, Gregory, A. [US/US]; 9729 Clagett Farm Drive, Potomac, MD 20854 (US). YU, Guo-Liang [CN/US]; 13524 Straw Bale Lane, Darnestown, MD 20878 (US). NI, Jian [CN/US]; 5502 Manorfield Road, Rockville, MD 20853 (US). FENG, Ping [CN/US]; 4 Relda Court, Gaithersburg, MD 20878 (US). YOUNG, Paul, E. [US/US]; 122 Beckwith Street, Gaithersburg, MD 20878 (US). GREENE, John, M. [US/US]; 872 Diamond Drive, Gaithersburg, MD 20878 (US). FERRIE, Ann, M. [US/US]; 13203 L Astoria Hill Court, Germantown, MD 20874 (US). DUAN, Roxanne [US/US]; 4541 Fairfield Drive, Bethesda, MD 20814 (US). HU, Jing-Shan [CN/US]; 1247 Lakeside Drive #3034, Sunnyvale, CA 94086 (US). GRAVES, Kimberly, A. [US/US]; 12805 Atlantic Avenue, Rockville, MD 20851 (US). OLSEN, Henrik, S. [DK/US]; 182 Kendrick Place #24, Gaithersburg, MD 20878 (US). EBNER, Reinhard [DE/US]; 9906 Shelburne Terrace #316, Gaithersburg, MD 20878 (US). BREWER, Laurie, A. [US/US]; 14920 Mt. Nebo Road, Poolesville, MD 20837 (US). MOORE, Paul, A. [GB/US]; Apartment #104, 1908 Holly Ridge Drive, McLean, VA 22102 (US). SHI, Yanggu [CN/US]; 437 West Side Drive, Gaithersburg, MD 20878 (US). LAFLEUR, David, W. [US/US]; 1615 Q Street, N.W. #807, Washington, DC 20009 (US). LI, Yi [CN/US]; 1247 Lakeside Drive #3034, Sunnyvale, CA 94086 (US). ZENG, Zhizhen [CN/US]; 13950 Saddleview Drive, Gaithersburg, MD 20878 (US). KYAW, Hla [BU/US]; 520 Sugarbush Circle, Frederick, MD 21703 (US). (74) Agents: BROOKES, Anders, A. et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 10850 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published With international search report. With an indication in relation to a deposited microorganism furnished under Rule 13 <sup>bi</sup> separately from the description. Date of receipt by the International Bureau: 06 April 1998 (06.04.98) (88) Date of publication of the international search report: 23 December 1998 (23.12.98)		60/040,162	7 March 1997 (07.03.97)	US	60/040,333	7 March 1997 (07.03.97)	US	60/038,621	7 March 1997 (07.03.97)	US	60/040,161	7 March 1997 (07.03.97)	US	60/040,626	7 March 1997 (07.03.97)	US	60/040,334	7 March 1997 (07.03.97)	US	60/040,336	7 March 1997 (07.03.97)	US	60/040,163	7 March 1997 (07.03.97)	US	60/043,580	11 April 1997 (11.04.97)	US	60/043,568	11 April 1997 (11.04.97)	US
60/040,162	7 March 1997 (07.03.97)	US																													
60/040,333	7 March 1997 (07.03.97)	US																													
60/038,621	7 March 1997 (07.03.97)	US																													
60/040,161	7 March 1997 (07.03.97)	US																													
60/040,626	7 March 1997 (07.03.97)	US																													
60/040,334	7 March 1997 (07.03.97)	US																													
60/040,336	7 March 1997 (07.03.97)	US																													
60/040,163	7 March 1997 (07.03.97)	US																													
60/043,580	11 April 1997 (11.04.97)	US																													
60/043,568	11 April 1997 (11.04.97)	US																													
(54) Title: 70 HUMAN SECRETED PROTEINS																															
(57) Abstract  The present invention relates to 70 novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.																															

60/043,314	11 April 1997 (11.04.97)	US	60/047,598	23 May 1997 (23.05.97)	US	60/056,882	22 August 1997 (22.08.97)	US
60/043,569	11 April 1997 (11.04.97)	US	60/047,613	23 May 1997 (23.05.97)	US	60/056,637	22 August 1997 (22.08.97)	US
60/043,311	11 April 1997 (11.04.97)	US	60/047,582	23 May 1997 (23.05.97)	US	60/056,903	22 August 1997 (22.08.97)	US
60/043,671	11 April 1997 (11.04.97)	US	60/047,596	23 May 1997 (23.05.97)	US	60/056,888	22 August 1997 (22.08.97)	US
60/043,674	11 April 1997 (11.04.97)	US	60/047,612	23 May 1997 (23.05.97)	US	60/056,879	22 August 1997 (22.08.97)	US
60/043,669	11 April 1997 (11.04.97)	US	60/047,632	23 May 1997 (23.05.97)	US	60/056,880	22 August 1997 (22.08.97)	US
60/043,312	11 April 1997 (11.04.97)	US	60/047,601	23 May 1997 (23.05.97)	US	60/056,894	22 August 1997 (22.08.97)	US
60/043,313	11 April 1997 (11.04.97)	US	60/047,595	23 May 1997 (23.05.97)	US	60/056,911	22 August 1997 (22.08.97)	US
60/043,672	11 April 1997 (11.04.97)	US	60/047,599	23 May 1997 (23.05.97)	US	60/056,636	22 August 1997 (22.08.97)	US
60/043,315	11 April 1997 (11.04.97)	US	60/047,588	23 May 1997 (23.05.97)	US	60/056,874	22 August 1997 (22.08.97)	US
60/043,578	11 April 1997 (11.04.97)	US	60/047,585	23 May 1997 (23.05.97)	US	60/056,910	22 August 1997 (22.08.97)	US
60/043,576	11 April 1997 (11.04.97)	US	60/047,586	23 May 1997 (23.05.97)	US	60/056,864	22 August 1997 (22.08.97)	US
60/043,670	11 April 1997 (11.04.97)	US	60/047,590	23 May 1997 (23.05.97)	US	60/056,631	22 August 1997 (22.08.97)	US
60/047,600	23 May 1997 (23.05.97)	US	60/047,594	23 May 1997 (23.05.97)	US	60/056,845	22 August 1997 (22.08.97)	US
60/047,615	23 May 1997 (23.05.97)	US	60/047,589	23 May 1997 (23.05.97)	US	60/056,892	22 August 1997 (22.08.97)	US
60/047,597	23 May 1997 (23.05.97)	US	60/047,593	23 May 1997 (23.05.97)	US	60/056,632	22 August 1997 (22.08.97)	US
60/047,502	23 May 1997 (23.05.97)	US	60/047,614	23 May 1997 (23.05.97)	US	60/056,664	22 August 1997 (22.08.97)	US
60/047,633	23 May 1997 (23.05.97)	US	60/047,501	23 May 1997 (23.05.97)	US	60/056,876	22 August 1997 (22.08.97)	US
60/047,583	23 May 1997 (23.05.97)	US	60/048,974	06 June 1997 (06.06.97)	US	60/056,881	22 August 1997 (22.08.97)	US
60/047,617	23 May 1997 (23.05.97)	US	60/048,964	06 June 1997 (06.06.97)	US	60/056,909	22 August 1997 (22.08.97)	US
60/047,618	23 May 1997 (23.05.97)	US	60/056,886	22 August 1997 (22.08.97)	US	60/056,875	22 August 1997 (22.08.97)	US
60/047,503	23 May 1997 (23.05.97)	US	60/056,877	22 August 1997 (22.08.97)	US	60/056,862	22 August 1997 (22.08.97)	US
60/047,592	23 May 1997 (23.05.97)	US	60/056,889	22 August 1997 (22.08.97)	US	60/056,887	22 August 1997 (22.08.97)	US
60/047,581	23 May 1997 (23.05.97)	US	60/056,893	22 August 1997 (22.08.97)	US	60/056,908	22 August 1997 (22.08.97)	US
60/047,584	23 May 1997 (23.05.97)	US	60/056,630	22 August 1997 (22.08.97)	US	60/056,884	22 August 1997 (22.08.97)	US
60/047,500	23 May 1997 (23.05.97)	US	60/056,878	22 August 1997 (22.08.97)	US	60/057,761	05 September 1997 (05.09.97)	US
60/047,587	23 May 1997 (23.05.97)	US	60/056,662	22 August 1997 (22.08.97)	US	60/057,650	05 September 1997 (05.09.97)	US
60/047,492	23 May 1997 (23.05.97)	US	60/056,872	22 August 1997 (22.08.97)	US			

# **FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

## INTERNATIONAL SEARCH REPORT

International Application No.

PC1/US 98/04482

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C12N5/10 C12N1/21 C07K14/47 C07K16/18  
C12Q1/68 G01N33/50 G01N33/53 G01N33/68 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>L. HILLIER ET AL.: "The WashU-Merck EST Project 1997" EMBL SEQUENCE DATABASE, 6 March 1997, HEIDELBERG, FRG, XP002068123 zr78g10.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 669570 5' similar to SW:FUCO_RAT P17164 Alpha-L-fucosidase precursor; Accession. Accession no. AA234924; ---</p> <p style="text-align: center;">-/--</p>	<p>1-3, 7-10,21</p>

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

16 June 1998

Date of mailing of the international search report

16. 09. 1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

HORNIG H.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/04482

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	L. HILLIER ET AL.: "The WashU-Merck EST Project" EMBL SEQUENCE DATABASE, 15 December 1996, HEIDELBERG, FRG, XP002068124 z140b11.r1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 504381 5' similar to TR:G182779 Lysosomal Enzyme Alpha-L-Fucosidase Accession no. AA151194 ---	1-3, 7-10,21
X	L. HILLIER ET AL.: "The WashU-Merck EST Project" EMBL SEQUENCE DATABASE, 4 June 1996, HEIDELBERG, FRG, XP002068125 zc54a02.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 326090 5' similar to SW:FUCO_HUMAN P4066 tissue Alpha-L-Fucosidase precursor; Accession no. W52490 ---	1-3, 7-10,21
A	WO 97 07198 A (GENETICS INSTITUT) 27 February 1997 see the whole document ---	1-23
A	WO 97 04097 A (GENETICS INST) 6 February 1997 see the whole document ---	1-23
A	US 5 536 637 A (JACOBS KENNETH) 16 July 1996 see the whole document ---	1-23
A	JACOBS K ET AL: "A novel method for isolating eukaryotic cDNA clones encoding secreted proteins." KEystone SYMPOSIUM ON DENDRITIC CELLS: ANTIGEN PRESENTING CELLS OF T AND B LYMPHOCYTES, TAOS, NEW MEXICO, USA, MARCH 10-16, 1995. JOURNAL OF CELLULAR BIOCHEMISTRY SUPPLEMENT 0 (21A). 1995. 19. ISSN: 0733-1959, XP002027246 abstract no. C1-207 see abstract ---	1-23
A	WO 90 14432 A (GENETICS INST) 29 November 1990 see the whole document ---	1-23
A	WO 96 17925 A (IMMUNEX CORP) 13 June 1996 see the whole document ---	1-23
	--- -/--	



## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 98/04482

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>T. OCCHIODORO ET AL.: "Human alpha-L-Fucosidase: Complete coding sequence from cDNA clones" BIOCHEM. AND BIOPHYS. RES. COMMUNICATIONS, vol. 164, no. 1, 16 October 1989, ACADEMIC PRESS, NEW YORK, US, pages 439-445, XP002068126 cited in the application see the whole document -----</p>	1-23

# INTERNATIONAL SEARCH REPORT

mational application No.

PCT/US 98/ 04482

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim 17 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see further information sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see further information sheet

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1. Claims: (1-23) partially

-An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence consisting of SEQ ID no. 11; wherein said polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein encoding the sequence of SEQ ID no. 134 or the polypeptide encoded by the cDNA sequence included in ATCC Deposit no: HGCMD20, which is hybridizable to SEQ ID no.11; a recombinant vector comprising said isolated nucleic acid molecule; a method of making a recombinant host cell comprising said isolated nucleic acid molecule; a recombinant host cell comprising said vector; an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence consisting of SEQ ID no. 134; an isolated antibody that binds specifically to said isolated polypeptide; a recombinant host cell that expresses said isolated polypeptide; a method of making said polypeptide; a method for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of said polypeptide; a method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject using said polynucleotide and/or polypeptide sequences; a method for identifying a binding partner to said polypeptide; a gene corresponding to the cDNA sequences of SEQ ID no.11; a method for identifying an activity in a biological assay, by using the expression of SEQ ID no. 134;

Inventions 2 to 70. Claims: (1-23) partially

-Idem as subject 1 but limited to gene nos. 2 to 70 respectively cDNA clone sequences HLDBG33 to HMCAB89.  
(Invention 2 is limited to SEQ ID nos.12,81,135, and 204;  
Invention 3 is limited to SEQ ID nos.13 and 136; .....;  
Invention 70 is limited to SEQ ID nos.80 and 203;)

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/04482

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9707198 A	27-02-97	US 5707829 A	13-01-98
		AU 6712396 A	18-02-97
		AU 6768596 A	12-03-97
		EP 0839196 A	06-05-98
		EP 0851875 A	08-07-98
		WO 9704097 A	06-02-97
WO 9704097 A	06-02-97	US 5707829 A	13-01-98
		AU 6712396 A	18-02-97
		EP 0839196 A	06-05-98
		AU 6768596 A	12-03-97
		EP 0851875 A	08-07-98
		WO 9707198 A	27-02-97
US 5536637 A	16-07-96	US 5712116 A	27-01-98
WO 9014432 A	29-11-90	US 5580753 A	03-12-96
		AT 147436 T	15-01-97
		AU 637620 B	03-06-93
		AU 5928990 A	18-12-90
		CA 2056997 A	24-11-90
		DE 69029657 D	20-02-97
		DK 473724 T	14-04-97
		EP 0473724 A	11-03-92
		ES 2099096 T	16-05-97
		JP 4506006 T	22-10-92
		US 5734037 A	31-03-98
		US 5414071 A	09-05-95
WO 9617925 A	13-06-96	AU 4639396 A	26-06-96
		CA 2206488 A	13-06-96
		FI 972390 A	05-06-97
		NO 972455 A	06-08-97



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : C12N 15/12, 5/10, 1/21, C07K 14/47, 16/18, C12Q 1/68, G01N 33/50, 33/53, 33/68, A61K 38/17		A2	(11) International Publication Number: <b>WO 98/39446</b>
			(43) International Publication Date: 11 September 1998 (11.09.98)
(21) International Application Number: PCT/US98/04482			
(22) International Filing Date: 6 March 1998 (06.03.98)			
(30) Priority Data:			
60/040,162	7 March 1997 (07.03.97)	US	
60/040,333	7 March 1997 (07.03.97)	US	
60/038,621	7 March 1997 (07.03.97)	US	
60/040,161	7 March 1997 (07.03.97)	US	
60/040,626	7 March 1997 (07.03.97)	US	
60/040,334	7 March 1997 (07.03.97)	US	
60/040,336	7 March 1997 (07.03.97)	US	
60/040,163	7 March 1997 (07.03.97)	US	
60/043,580	11 April 1997 (11.04.97)	US	
60/043,568	11 April 1997 (11.04.97)	US	
(Continued on the following page)			
(71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).		(74) Agents: BROOKES, Anders, A. et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 10850 (US).	
(72) Inventors; and			
(75) Inventors/Applicants (for US only): RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). FISCHER, Carrie, L. [US/US]; 5810 Hall Street, Burke, VA 22015 (US). SOPER, Daniel, R. [US/US]; 15050 Stillfield Place, Centreville, VA 22020 (US). CARTER, Kenneth, C. [US/US]; 11601 Brandy Hall Lane, North Potomac, MD 20878 (US). BEDNARIK, Daniel, P. [US/US]; 8822 Blue Sea Drive, Columbia, MD 21046 (US). ENDRESS, Gregory, A. [US/US]; 9729 Clagett Farm Drive, Potomac, MD 20854 (US). YU, Guo-Liang [CN/US]; 13524 Straw Bale Lane, Darnestown, MD 20878 (US). NI, Jian [CN/US]; 5502 Manorfield Road, Rockville, MD 20853 (US). FENG, Ping [CN/US]; 4 Reida Court, Gaithersburg, MD 20878 (US). YOUNG, Paul, E. [US/US]; 122 Beckwith Street, Gaithersburg, MD 20878 (US). GREENE, John, M. [US/US]; 872 Diamond Drive, Gaithersburg, MD 20878 (US). FERRIE, Ann, M. [US/US]; 13203 L Astoria Hill Court, Germantown, MD 20874 (US). DUAN, Roxanne [US/US]; 4541 Fairfield Drive, Bethesda,		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).	
		Published Without international search report and to be republished upon receipt of that report. With an indication in relation to a deposited microorganism furnished under Rule 13bis separately from the description. Date of receipt by the International Bureau: 06 April 1998 (06.04.1998)	
(54) Title: 70 HUMAN SECRETED PROTEINS			
(57) Abstract			
The present invention relates to 70 novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.			

60/043,314	11 April 1997 (11.04.97)	US	60/047,598	23 May 1997 (23.05.97)	US	60/056,882	22 August 1997 (22.08.97)	US
60/043,569	11 April 1997 (11.04.97)	US	60/047,613	23 May 1997 (23.05.97)	US	60/056,637	22 August 1997 (22.08.97)	US
60/043,311	11 April 1997 (11.04.97)	US	60/047,582	23 May 1997 (23.05.97)	US	60/056,903	22 August 1997 (22.08.97)	US
60/043,671	11 April 1997 (11.04.97)	US	60/047,596	23 May 1997 (23.05.97)	US	60/056,888	22 August 1997 (22.08.97)	US
60/043,674	11 April 1997 (11.04.97)	US	60/047,612	23 May 1997 (23.05.97)	US	60/056,879	22 August 1997 (22.08.97)	US
60/043,669	11 April 1997 (11.04.97)	US	60/047,632	23 May 1997 (23.05.97)	US	60/056,880	22 August 1997 (22.08.97)	US
60/043,312	11 April 1997 (11.04.97)	US	60/047,601	23 May 1997 (23.05.97)	US	60/056,894	22 August 1997 (22.08.97)	US
60/043,313	11 April 1997 (11.04.97)	US	60/047,595	23 May 1997 (23.05.97)	US	60/056,911	22 August 1997 (22.08.97)	US
60/043,672	11 April 1997 (11.04.97)	US	60/047,599	23 May 1997 (23.05.97)	US	60/056,636	22 August 1997 (22.08.97)	US
60/043,315	11 April 1997 (11.04.97)	US	60/047,588	23 May 1997 (23.05.97)	US	60/056,874	22 August 1997 (22.08.97)	US
60/043,578	11 April 1997 (11.04.97)	US	60/047,585	23 May 1997 (23.05.97)	US	60/056,910	22 August 1997 (22.08.97)	US
60/043,576	11 April 1997 (11.04.97)	US	60/047,586	23 May 1997 (23.05.97)	US	60/056,864	22 August 1997 (22.08.97)	US
60/043,670	11 April 1997 (11.04.97)	US	60/047,590	23 May 1997 (23.05.97)	US	60/056,631	22 August 1997 (22.08.97)	US
60/047,600	23 May 1997 (23.05.97)	US	60/047,594	23 May 1997 (23.05.97)	US	60/056,845	22 August 1997 (22.08.97)	US
60/047,615	23 May 1997 (23.05.97)	US	60/047,589	23 May 1997 (23.05.97)	US	60/056,892	22 August 1997 (22.08.97)	US
60/047,597	23 May 1997 (23.05.97)	US	60/047,593	23 May 1997 (23.05.97)	US	60/056,632	22 August 1997 (22.08.97)	US
60/047,502	23 May 1997 (23.05.97)	US	60/047,614	23 May 1997 (23.05.97)	US	60/056,664	22 August 1997 (22.08.97)	US
60/047,633	23 May 1997 (23.05.97)	US	60/047,501	23 May 1997 (23.05.97)	US	60/056,876	22 August 1997 (22.08.97)	US
60/047,583	23 May 1997 (23.05.97)	US	60/048,974	06 June 1997 (06.06.97)	US	60/056,881	22 August 1997 (22.08.97)	US
60/047,617	23 May 1997 (23.05.97)	US	60/048,964	06 June 1997 (06.06.97)	US	60/056,909	22 August 1997 (22.08.97)	US
60/047,618	23 May 1997 (23.05.97)	US	60/056,886	22 August 1997 (22.08.97)	US	60/056,875	22 August 1997 (22.08.97)	US
60/047,503	23 May 1997 (23.05.97)	US	60/056,877	22 August 1997 (22.08.97)	US	60/056,862	22 August 1997 (22.08.97)	US
60/047,592	23 May 1997 (23.05.97)	US	60/056,889	22 August 1997 (22.08.97)	US	60/056,887	22 August 1997 (22.08.97)	US
60/047,581	23 May 1997 (23.05.97)	US	60/056,893	22 August 1997 (22.08.97)	US	60/056,908	22 August 1997 (22.08.97)	US
60/047,584	23 May 1997 (23.05.97)	US	60/056,630	22 August 1997 (22.08.97)	US	60/056,884	22 August 1997 (22.08.97)	US
60/047,500	23 May 1997 (23.05.97)	US	60/056,878	22 August 1997 (22.08.97)	US	60/057,761	05 September 1997 (05.09.97)	US
60/047,587	23 May 1997 (23.05.97)	US	60/056,662	22 August 1997 (22.08.97)	US	60/057,650	05 September 1997 (05.09.97)	US
60/047,492	23 May 1997 (23.05.97)	US	60/056,872	22 August 1997 (22.08.97)	US			

# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CJ	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LJ	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

## 70 Human Secreted Proteins

### *Field of the Invention*

This invention relates to newly identified polynucleotides and the polypeptides encoded by these polynucleotides, uses of such polynucleotides and polypeptides, and  
5 their production.

### *Background of the Invention*

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or  
10 organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum  
15 (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

20 Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or  
25 secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include  
30 the commercially valuable human insulin, interferon, Factor VIII, human growth hormone, tissue plasminogen activator, and erythropoietin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical disorders by using  
35 secreted proteins or the genes that encode them.

### *Summary of the Invention*

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting disorders related to the polypeptides, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying binding partners of the polypeptides.

### *Detailed Description*

#### **Definitions**

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide.

In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X or the cDNA contained within the clone deposited with the ATCC. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without the signal sequence, the secreted protein coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having the translated amino acid sequence generated from the polynucleotide as broadly defined.

In the present invention, the full length sequence identified as SEQ ID NO:X was often generated by overlapping sequences contained in multiple clones (contig



analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X was deposited with the American Type Culture Collection ("ATCC"). As shown in Table 1, each clone is identified by a cDNA Clone ID (Identifier) and the ATCC Deposit Number. The ATCC is located at 12301 Park Lawn Drive, Rockville, Maryland 20852, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, the complement thereof, or the cDNA within the clone deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42°C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH<sub>2</sub>PO<sub>4</sub>; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 µg/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA<sup>+</sup> sequences (such as any 3' terminal polyA<sup>+</sup> tract of a cDNA shown in the sequence listing), or to a

complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone).

5           The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and  
10   double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability  
15   or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

          The polypeptide of the present invention can be composed of amino acids joined  
20   to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs,  
25   as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be  
30   branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a  
35   nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine,

formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

"SEQ ID NO:X" refers to a polynucleotide sequence while "SEQ ID NO:Y" refers to a polypeptide sequence, both sequences identified by an integer specified in Table 1.

"A polypeptide having biological activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention.)

## **Polynucleotides and Polypeptides of the Invention**

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 1**

The translation product of Gene NO: 1 shares sequence homology with alpha-L-fucosidase which is thought to be important as a lysosomal enzyme that hydrolyzes fucose from fucoglycoconjugates. (See Accession No. gi/178409.) Lysosome fructosidase is involved in certain lysosome storage diseases. (See Biochem. Biophys. Res. Commun., 164(1):439-445 (1989).) Fucosidosis, an autosomal recessive lysosomal storage disorder characterized by progressive neurological deterioration and mental retardation. The disease results from deficient activity of alpha-L-fucosidase, a lysosomal enzyme that hydrolyzes fucose from fucoglycoconjugates. This gene likely encodes a novel fucosidase isoenzyme. Based on homology, it is likely that the translated product of this gene is also involved in lysosome catabolism of molecules and

that aberrations in the concentration and/or composition of this product may be causative in lysosome storage disorders. Preferred polypeptide fragments comprise the amino acid sequence PGHLLPHKWENC (SEQ ID NO: 257).

Gene NO: 1 is expressed primarily in stromal cells, and to a lesser extent in  
5 human fetal kidney and human tonsils.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, fucosidosis and other lysosome storage disorders. Similarly,  
10 polypeptides and antibodies directed to the polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues of cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., stromal cells, kidney, tonsils, and cancerous and  
15 wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology of Gene NO: 1 to alpha-L-fucosidase  
20 indicates that polypeptides and polynucleotides corresponding to Gene NO: 1 are useful for the treatment of fucosidosis and general lysosomal disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 134 as residues: Met-1 to Leu-6, Thr-32 to Glu-39, Lys-80 to Lys-85, and Met-90 to Pro-96.  
25

## **FEATURES OF PROTEIN ENCODED BY GENE NO: 2**

The translation product of Gene No. 2 shares sequence homology with stromal cell-derived factor-2 (SDF-2) which is a novel secreted factor. See, for example, Gene, 176(1-2):211-214, (1996, Oct. 17.) The amino acid sequence of SDF-2 shows  
30 similarity to yeast dolichyl phosphate-D-mannose:protein mannosyltransferases, Pmt1p [Strahl-Bolsinger et al. Proc. Natl. Acad. Sci. USA 90, 8164-8168 (1993)] and Pmt2p [Lussier et al. J. Biol. Chem. 270, 2770-2775 (1995)], whose activities have not been detected in higher eukaryotes. Based on the sequence similarity, the translation product of this gene is expected to share certain biological activities with SDF-2, Pmt1p and  
35 Pmt2p.

Gene NO: 2 is expressed primarily in immune system tissue and cancerous tissues, such as liver hepatoma, human B-cell lymphoma, spleen in a patient suffering

from chronic lymphocytic leukemia, hemangiopericytoma, pharynx carcinoma, breast cancer, thyroid, bone marrow, osteoblasts and to a lesser extent in a few other tissues such as kidney pyramids.

Therefore, polynucleotides or polypeptides of the invention are useful as  
5 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of the diseases and conditions which include, but are not limited to, disorders in kidney, liver, and immune organs, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell  
10 type(s). For a number of disorders of the above tissues or cells, particularly of the kidney, liver, thyroid, and bone marrow expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., liver, spleen, B-cells, pharynx, thyroid, mammary tissue, bone marrow, osteoblasts and kidneys, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma,  
15 urine, synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology of Gene NO: 2 to stromal cell-derived  
20 factor-2 indicates that polypeptides and polynucleotides corresponding to Gene NO: 2 are useful for diagnosis and therapeutic treatment of disorders in kidney, liver, and immune organs since stromal cells play important role in organ function. Stroma carries the blood supply and provides support for the growth of parenchymal cells and is therefore crucial to the growth of a neoplasm. Nucleic acids of the present invention  
25 comprise, but preferably do not consist of, and more preferably do not comprise, SEQ ID NO: 3 from US Patent No. 5,576,423, incorporated herein by reference, and shown herein as SEQ ID NO: 258).

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
135 as residues: His-56 to Gly-65, Ala-74 to Ser-80, Ile-84 to Pro-97, Leu-124 to Glu-  
30 129, Glu-135 to Asp-143, Gly-175 to Ser-180, and Ala-194 to Thr-199.

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 3**

The translation product of Gene NO: 3 shares sequence homology with LZIP-1,  
LZIP-2 and other leucine zipper proteins, which are thought to be important in nucleic  
35 acid binding. This gene has been reported in Mol. Cell. Biol. 17 (9), 5117-5126 (1997) as "Luman". Luman is a cyclic AMP response element (CRE)-binding protein/activating transcription factor 1 protein of the basic leucine zipper superfamily. It binds CREs in

vitro and activates CRE-containing promoters when transfected into COS7 cells. The complete amino acid sequence of Luman reported in Mol. Cell. Biol. 17 (9): 5117-5126 (1997) is:

MELELDAGDQDLLAFLLEESGDLGTAPDEAVRAPLDWALPLSEVPSDWEVDDLL  
 5 CSLLSPPASLNILSSSNPCLVHHDHTYSLPRETVSMDLESESCRKEGTQMTPQH  
 MEELAEQEIARLVLTDEEKSLLKEGLILPETLPLTKTEEQILKRVRRKIRNKRSA  
 QESRRKKKVYVGGLESRLKYTAQNMEQLQNKVQLLEEQLNSLLDQLRKLQAM  
 VIEISNKTSSSSTCILVLLVSFCLLLVPAMYSSDTRGSLPAEHGVLSRQLRALPSE  
 DPYQLELPAHQSEVPKSTHQWLDGSDCVLQAPGNTSCLLHYMPQAPSAEPPL  
 10 EWPFDDLSS EPLCRGPILPLQANLTRKGGWLPTGSPSVILQDRYSG (SEQ ID  
 N:259).

Gene NO: 3 is expressed primarily in apoptotic T-cells and Soares senescent cells and to a lesser extent in multiple tissues and cell types, including, multiple sclerosis tissue, and hippocampus.

15 Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunologically mediated disorders, transplantation, immunodeficiency, and tumor necrosis. Similarly, polypeptides and antibodies directed to these  
 20 polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and transplantation, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., multiple sclerosis tissue, hippocampus, bone marrow and cancerous and wounded  
 25 tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology of Gene NO: 3 to leucine zipper nucleic  
 30 acid binding proteins indicates that polypeptides and polynucleotides corresponding to Gene NO: 3 are useful for diagnosis and treatment of immunologically mediated disorders, transplantation, immunodeficiency, and tumor necrosis. The secreted nucleic acid binding protein in the apoptotic tissues may be involved in the disposal of the DNA released by apoptotic cells. Furthermore, the studies conducted in support of Luman  
 35 suggest that the translation product of this gene may be used to identify transcriptional regulation elements which in turn are useful in modulation of immune function.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 136 as residues: Asn-7 to Ser-12, Tyr-32 to Gly-38, Pro-55 to Tyr-60, Glu-70 to Thr-76, and Pro-104 to Leu-110.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 4

The translation product of Gene NO: 4 shares sequence homology with a number of tetraspan transmembrane surface molecules such as human metastasis tumor suppressor gene, CO-029 tumor associated antigen protein, CD53 hematopoietic antigen, human membrane antigen TM4 superfamily protein, metastasis controlling  
10 peptide, and human CD9 sequence, which are thought to be important in development of cancer, immune system development and functions.

Gnee NO: 4 is expressed primarily in cancers of several different tissues and to a lesser extent in normal tissue like prostate, skin and kidney.

Therefore, polynucleotides or polypeptides of the invention are useful as  
15 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers and disorders of the immune system, prostate and kidney. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell  
20 type(s). For a number of disorders of the above tissues or cells, particularly of the kidney, skin, prostate and immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., kidney, skin and prostate, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from  
25 an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology of Gene NO: 4 to tetraspan transmembrane surface molecules such as human metastasis tumor suppressor gene,  
30 CO-029 tumor associated antigen protein, CD53 hematopoietic antigen, human membrane antigen TM4 superfamily protein, metastasis controlling peptide, and human CD9 sequence, indicates that polypeptides and polynucleotides corresponding to Gene NO: 4 are involved with the cellular control of growth and differentiation. Therefore, the translation product of this gene is believed to be useful for diagnosis and treatment  
35 of neoplasia and disorders of the kidney, skin and prostate. For example, recombinant protein can be produced in transformed host cells for diagnostic and prognostic applications. Alterations in the protein sequence are indicative of the presence of

malignant cancer, or of a predisposition to malignancy, in a subject. Gene therapy can be used to restore the wild-type gene product to a subject. Additionally, the antibodies are a useful tool for the identification of hematopoietic neoplasms, and may prove helpful for identifying morphologically poorly defined cells. Moreover, this protein can be used to isolate cognate receptors and ligands and identify potential agonists and antagonists using techniques known in the art. The protein also has immunomodulatory activity, regulates hematopoiesis and stimulates growth and regeneration as a male/female contraceptive, increases fertility depending on activin and inhibin like activities. Other uses are as a chemotactic agent for lymphocytes, treatment of coagulation disorders, an anti-inflammatory agent, an antimicrobial or analgesic and as a modulator of behavior and metabolism. The DNA can be used in genetic diagnosis or gene therapy, and for the production of recombinant protein. It can also be used to identify protein expressing cells, isolate related sequences, prepare primers for genetic fingerprinting and generate anti-protein or anti-DNA antibodies. In addition, residues 1-71, in the translation product for this gene are believed to be the extracellular domain. Thus, polypeptide comprising residues 1-71 or derivatives (including fragments) or analogs thereof, are useful as a soluble polypeptide which may be routinely used therapeutically to antagonize the activities of the receptor.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 137 as residues: Lys-118 to Phe-127, Asn-145 to Ala-160, and Thr-177 to Val-188.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 5**

Gene NO: 5 is expressed primarily in human testes.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the testes including cancer and reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., testes and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.



The tissue distribution of Gene NO: 5 indicates that the protein product of this gene is useful for treatment/diagnosis of diseases of the testes, particularly testicular cancer since expression is observed primarily in the testes.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
5 138 as residue: Gly-22 to Gln-30.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 6**

The translation product of Gene NO: 6 shares sequence homology with GALNS (N-acetylgalactosamine 6-sulphatase) which is thought to be important in the storage of  
10 the glycosaminoglycans, keratan sulfate and chondroitin 6-sulfate. See Genbank accession no. gil618426. Based on the sequence similarity, the translation product of this gene is expected to share biological activities with GALNS.

Gene NO: 6 is expressed primarily in human bone marrow.

Therefore, polynucleotides or polypeptides of the invention are useful as  
15 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, storage disorders of glycosaminoglycans, keratan sulfate and chondroitin 6-sulfate, e.g., Morquio A syndrome. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential  
20 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly involving cell storage disorder, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., bone marrow and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from  
25 an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology of Gene NO: 6 to N-acetylgalactosamine 6-sulphatase indicates that polypeptides and polynucleotides corresponding to Gene  
30 NO: 6 are useful for the treatment and diagnosis of storage disorders of glycosaminoglycans, keratan sulfate and chondroitin 6-sulfate. Such disorders are known in the art and include, e.g., Morquio A syndrome which is caused by an error of mucopolysaccharide metabolism with excretion of keratan sulfate in urine. Morquio A syndrome is characterized by severe skeletal defects with short stature, severe deformity  
35 of spine and thorax, long bones with irregular epiphyses but with shafts of normal length, enlarged joints, flaccid ligaments, and waddling gait; autosomal recessive inheritance.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 139 as residues: Gly-29 to Pro-36 and Glu-57 to Leu-64.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 7**

5       The translation product of Gene NO: 7 shares sequence homology with carboxy peptidase E and H (carboxypeptidase E is thought to be important in the biosynthesis of numerous peptide hormones and neurotransmitters). The translation product of this gene also shares sequence homology with bone-related carboxypeptidase "OSF-5" from the mouse. See European patent application EP-588118-A. Based on the sequence  
10 similarity to OSF-5, the translation product of this gene will hereinafter sometimes be referred to as "human-OSF-5" or "hOSF-5".

Gene NO: 7 is expressed primarily in tumor cell lines derived from connective tissues including chondrosarcoma, synovial sarcoma, Wilm's tumor and rhabdomyosarcoma and to a lesser extent in a myeloid progenitor cell line, bone  
15 marrow, and placenta.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, various cancers involving the skeletal system and connective tissues in  
20 general, in particular at cartilage interfaces. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system and various other tumor tissues, expression of this gene at significantly higher or lower levels may routinely be  
25 detected in certain tissues (e.g., connective tissues and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

30       The restricted tissue distribution and homology of Gene NO: 7 to carboxypeptidase E and mouse OSF-5 indicates that polypeptides and polynucleotides corresponding to Gene NO: 7 are for processing of peptides to their mature form that may have various activities similar to the activities of neuropeptides but in the periphery. In addition the abundance of expression in cancer tissues indicates that  
35 aberrant expression and subsequent processing may play a role in the progression of malignancies, e.g., growth factor and/or adhesion factor activities. In particular, the expression of this gene is restricted to connective tissues and embryonic tissues.

Furthermore, it is overexpressed in cancers of these same tissues (i.e., in sarcomas). Moreover, hOSF-5 shares very strong sequence similarity with mOSF-5 which is a known bone growth factor and is thought to be useful in obtaining products for the diagnosis and treatment of bone metabolic diseases, e.g., osteoporosis and Paget's disease. Like OSF-5, the translation product of this gene is believed to be a bone-specific carboxypeptidase which acts as an adhesion molecule/growth factor and takes part in osteogenesis at the site of bone induction. hOSF-5 can, therefore, be used to treat bone metabolic diseases, osteoporosis, Paget's disease, osteomalacia, hyperostosis or osteopetrosis. Furthermore, hOSF-5 can be used to stimulate the regeneration of bone at the site of mechanical damage, e.g., accidentally or surgically caused fractures.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 140 as residues: Leu-24 to Val-30, Ala-89 to Lys-94, Phe-150 to Trp-157, Leu-162 to Asp-167, Asp-187 to Ser-199, His-241 to Asp-254, and Pro-362 to Asp-376.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 8**

Gene NO: 8 is expressed primarily in bone marrow, and to a lesser extent in an erythroleukemia cell line.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematological disorders including cancer and anemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematologic systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., bone marrow, kidney, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 8 are useful as a growth factor for hematopoietic stem cells or progenitor cells, e.g., in the treatment of bone marrow stem cell loss in chemotherapy patients and in the treatment of kidney disease.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 141 as residues: Gly-30 to Lys-35.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 9**

Gene NO: 9 is expressed primarily in neutrophils.

Therefore, polynucleotides or polypeptides of the invention are useful as  
5 reagents for differential identification of the cell type present in a biological sample and  
for diagnosis of diseases and conditions which include, but are not limited to,  
inflammatory diseases. Similarly, polypeptides and antibodies directed to these  
polypeptides are useful in providing immunological probes for differential identification  
of the cell type indicated. For a number of disorders of the above tissues or cells,  
10 particularly of the immune system, expression of this gene at significantly higher or  
lower levels may routinely be detected in certain tissues or cell types (e.g., neutrophils,  
bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from  
an individual having such a disorder, relative to the standard gene expression level, i.e.,  
15 the expression level in healthy tissue or bodily fluid from an individual not having the  
disorder.

The tissue distribution indicates that polypeptides and polynucleotides  
corresponding to Gene NO: 9 are useful for immune modulation or as a growth factor  
to stimulate neutrophil differentiation or proliferation that may be useful in the treatment  
20 of neutropenia.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
142 as residues: Thr-22 to Pro-37.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 10**

25 Gene NO: 10 is expressed primarily in the epidermis.

Therefore, polynucleotides or polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of diseases and conditions which include, but are  
not limited to, diseases of the epidermis such as psoriasis or eczema or may be involved  
30 in the normal proliferation or differentiation of the epithelial cells or fibroblasts  
constituting the skin. Similarly, polypeptides and antibodies directed to these  
polypeptides are useful in providing immunological probes for differential identification  
of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,  
particularly of the skin, expression of this gene at significantly higher or lower levels  
35 may routinely be detected in certain tissues (e.g., epidermis and cancerous and  
wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal  
fluid) or another tissue or cell sample taken from an individual having such a disorder,

relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 10 are useful for diagnosis and treatment of skin conditions and as an aid in the healing of various epidermal injuries including wounds, and diabetic ulcers.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 143 as residues: Ser-3 to Ser-9 and Trp-27 to Glu-32.

## 10 FEATURES OF PROTEIN ENCODED BY GENE NO: 11

The translation product of Gene NO: 11 shares sequence homology with phosphatidylcholine 2-acylhydrolase (PLA2). See, for example, Genbank accession no. g1190004. PLA2 is involved in inflammation, where it is responsible for the conversion of cell membrane phospholipids into arachidonic acid. Arachidonic acid in turn feeds into both the lipoxygenase and cyclooxygenase pathways to produce leukotrienes (involved in chemotaxis, vasoconstriction, bronchoconstriction, and increased vascular permeability) and prostaglandins (responsible for vasodilation, potentiate edema, and increased pain). Diseases in which PLA2 is implicated as a major factor include rheumatoid arthritis, sepsis, ischemia, and thrombosis. The inventors refer to the translation product of this gene as PLA2-like protein based on the sequence similarity. Furthermore, owing to the sequence similarity PLA2 and PLA2-like protein are expected to share certain biological activities.

Gene NO: 11 is expressed primarily in human cerebellum and in T-cells.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cerebellum disorders, rheumatoid arthritis, sepsis, ischemia, and thrombosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cerebellum and Purkinje cells, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., brain, bone marrow, T-cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 11 are useful for diagnosis and treatment of cerebellum disorders, rheumatoid arthritis, sepsis, ischemia, and thrombosis. This gene is also useful as a chromosome marker. It is believed to map to Chr.15, D15S118-D15S123.

5

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 12**

Gene NO: 12 is expressed primarily in highly vascularized tissues such as placenta, uterus, tumors, fetal liver, fetal spleen and also in the C7MCF7 cell line treated with estrogen.

10 Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endometriosis, endometritis, endometrial carcinoma, primary hepatocellular carcinoma, and spleen-related diseases. Similarly, polypeptides and  
15 antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endometrium, liver and spleen, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., endometrium, liver, and spleen, and cancerous and wounded  
20 tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides  
25 corresponding to Gene NO: 12 are useful for diagnosis and treatment of diseases of the endometrium (such as endometrial carcinoma, endometriosis, and endometritis), liver diseases (such as primary hepatocellular carcinoma), and spleen-related diseases.

SEQ ID NO: 145 as residues: Ala-29 to Leu-35, Leu-50 to Ser-57, Glu-96 to Glu-105, Asp-140 to Asp-148, and Asn-191 to Ser-197.

30

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 13**

Gene NO: 13 is expressed primarily in B cell lymphoma and to a lesser extent in other tissues.

35 Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, B cell lymphoma; hematopoietic disorders; immune dysfunction.

Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may  
5 routinely be detected in certain tissues and cell types (e.g., bone marrow and B-cells and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the  
10 disorder.

Enhanced expression of this gene product in B cell lymphoma indicates that it may play a role in the proliferation of hematopoietic cells. It is also believed to be involved in the survival and/or differentiation of various hematopoietic lineages. Expression in lymphoma also indicates that it may be involved in other cancers and  
15 abnormal cellular proliferation. The tissue distribution, therefore, indicates that polypeptides and polynucleotides corresponding to Gene NO: 13 are useful for the diagnosis and/or therapeutic treatment of hematopoietic disorders, particularly B cell lymphoma. Furthermore, since overexpression of this gene is associated with the development of B cell lymphoma, antagonists of this protein are useful to interfere with  
20 the progression of the disease. This protein is useful in assays for identifying such antagonists. Assays for identifying antagonists are known in the art and are described briefly elsewhere herein. Preferred antagonists include antibodies and antisense nucleic acid molecules. Preferred are antagonists which inhibit B-cell proliferation.

## 25 **FEATURES OF PROTEIN ENCODED BY GENE NO: 14**

The translation product of Gene NO: 14 shares sequence homology with very low density lipoprotein receptor which is thought to be important in transport of lipoproteins. Owing to the sequence similarity the translation product of this gene is believed to share certain biological activities with VLDL receptors. Assaying such  
30 activity may be achieved by assays known in the art and set forth elsewhere herein.

This gene is expressed primarily in human synovium, umbilical vein endothelial cells, CD34+ cells, Jurkat cells, and HL60 cells, and to a lesser extent in thymus, meningioma, hypothalamus, adult testis, and fetal liver and spleen.

Therefore, polynucleotides or polypeptides of the invention are useful as  
35 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, atherosclerosis, ataxia malabsorption, vascular damage, hyperlipidemia,

and other cardiovascular diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular and hematological systems,

5 expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., endothelium, thymus meningioma, hypothalamus, testes, liver, and spleen and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e.,  
10 the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in the vascular endothelial cells and homology to VLDL receptors indicates that polypeptides and polynucleotides corresponding to Gene NO: 14 are useful for diagnosis and treatment of atherosclerosis, ataxia malabsorption, and  
15 hyperlipidemia. These and other factors often result in other cardiovascular diseases. Additionally, the presence of the gene product in cells of blood lineages indicates that it may be useful in hematopoietic regulation and hemostasis.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 147 as residues: Pro-39 to Ser-52, Trp-71 to Thr-76, and Pro-94 to His-100.

20

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 15**

The translation product of Gene NO: 15 shares sequence homology with kallikrein which is thought to be important in blood pressure and renal secretion. Furthermore, this gene has now been characterized as a novel hepatitis B virus X  
25 binding protein that inhibits viral replication. See, for example, J. Virol. 72 (3), 1737-1743 (1998).

This gene is expressed primarily in kidney, placenta, lung, aorta and other endothelial cells, caudate nucleus and to a lesser extent in melanocytes, liver, adipose tissue.

30 Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renovascular hypertension, renal secretion, electrolyte metabolism, toxemia of pregnancy. Similarly, polypeptides and antibodies directed to these  
35 polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renovascular or respiratory vascular systems, expression of this gene



at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., kidney, placenta, lung, endothelial cells, melanocytes, liver, and adipose tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to kallikrein indicates that polypeptides and polynucleotides corresponding to Gene NO: 15 are useful for treating renovascular hypertension, renal secretion, electrolyte metabolism, toxemia of pregnancy and hydronephrosis. The protein expression in the organs like kidney, lung and vascular endothelial cells indicates the gene involvement in hemodynamic regulatory functions. The translation product of this gene is also useful in the treatment of viral infection, particularly liver infection, and particularly hepatitis B virus(es).

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 148 as residues: Leu-9 to Asn-15 and Thr-56 to Asp-61.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 16**

The translation product of Gene NO: 16 shares sequence homology with secretory component protein, immunoglobulins and their receptors which are thought to be important in immunological functions. The amino acid sequence of secretory component protein can be accessed as accession no. pirlA02112, incorporated herein by reference.

Gene NO: 16 is expressed primarily in macrophages, monocytes and dendritic cells and to a lesser extent in placenta and brain.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and tumors. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues or cells (e.g., macrophages, monocytes, dendritic cells, placenta and brain, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a

disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to immunoglobulins and secretory component protein indicates that polypeptides and polynucleotides corresponding to  
5 Gene NO: 16 are useful for diagnosis and treatment of inflammation and bacterial infection, and other diseases where immunomodulation would be beneficial.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 149 as residues: Pro-37 to Cys-51, Gln-53 to Cys-60, Asn-99 to Gly-106, Gly-145 to Glu-151, and Ile-159 to Ser-164.

10

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 17**

The translation product of Gene NO: 17 is evolutionarily conserved and shares sequence homology with proteins from yeast and *C. elegans*. See, for example, Genbank accession no.gi746540. As is known in the art, strong sequence similarity to  
15 a secreted protein from *C. elegans* is predictive of cellular location of human proteins.

Gene NO: 17 is expressed primarily in colon carcinoma cell lines, messangial cells, many tumors like T cell lymphoma, osteoclastoma, Wilm's tumor, adrenal gland tumor, testes tumor, synovial sarcoma, and to a lesser extent in placenta, lung and brain.

20 Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, rapidly growing/dividing cells such as cancerous tissue, including, colon carcinoma, lymphomas, and sarcomas. Similarly, polypeptides and antibodies directed  
25 to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the gastrointestinal, hematological and immune systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., placenta, lung, brain, colon, messangial cells,  
30 adrenal gland, T-cells, testes, and lymph tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

35 The tissue distribution in colon cancer and many other tumors indicates that the polynucleotides and polypeptides of Gene NO: 17 are useful for cancer diagnosis and therapeutic targeting. The extracellular nature may contribute to solid tumor

immunosuppression, angiogenesis and cell growth stimulation. The tissue distribution of this gene in cells of the immune system indicates that polypeptides and polynucleotides corresponding to Gene NO: 17 are useful for treatment, prophylaxis and diagnosis of immune and autoimmune diseases, such as lupus, transplant rejection, allergic reactions, arthritis, asthma, immunodeficiency diseases, leukemia, and AIDS. Its expression predominantly in hematopoietic cells also indicates that the gene could be important for the treatment and/or detection of hematopoietic disorders such as graft versus host reaction, graft versus host disease, transplant rejection, myelogenous leukemia, bone marrow fibrosis, and myeloproliferative disease. The protein can also be used to enhance or protect proliferation, differentiation and functional activation of hematopoietic progenitor cells such as bone marrow cells, which could be useful for cancer patients undergoing chemotherapy or patients undergoing bone marrow transplantation. The protein may also be useful to increase the proliferation of peripheral blood leukocytes, which could be useful in the combat of a range of hematopoietic disorders including immunodeficiency diseases, leukemia, and septicemia.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 150 as residues: Val-131 to Asn-136.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 18**

The translation product of Gene NO: 18 shares sequence homology with immunoglobulin, which is thought to be important in immunoreactions.

Gene NO: 18 is expressed primarily in macrophage.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., macrophage and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in macrophages and the weak homology to immunoglobulin indicates that polypeptides and polynucleotides corresponding to Gene

NO: 18 are useful for diagnosing and treating immune response disorders, including inflammation, antigen presentation and immunosurveillance.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 19**

5       The translation product of Gene NO: 19 shares sequence homology with proline rich proteins which are thought to be important in protein-protein interaction.

      This gene has a wide range of tissue distribution, but is expressed primarily in normal prostate, synovial fibroblasts, brain amygdala depression, fetal bone and fetal cochlea, and to a lesser extent in adult retina, umbilical vein endothelial cells, atrophic  
10      endometrium, osteoclastoma, melanocytes, pancreatic carcinoma and smooth muscle.

      Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer metastasis, wound healing, tissue repair. Similarly, polypeptides  
15      and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal, connective tissues, reproductive and central nervous system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., brain,  
20      prostrate, fibroblasts, bone, cochlea, retina, endothelial cells, endometrium, pancreas and smooth muscle, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the  
25      disorder.

      The tissue distribution and homology to proline-rich proteins indicates that the protein is a extracellular matrix protein or an ingredient of bodily fluid. Polypeptides and polynucleotides corresponding to Gene NO: 19 are useful for cancer metastasis intervention, tissue culture additive, bone modeling, wound healing and tissue repair.  
30

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 20**

      Gene NO: 20 is expressed primarily in prostate cancer, leukocytes, meningima, adult liver, pancreas, brain, and to a lesser extent in lung.

      Therefore, polynucleotides or polypeptides of the invention are useful as  
35      reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate cancers. Similarly, polypeptides and antibodies directed to these

polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate and brain, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., prostate, leukocytes, meningioma, liver, brain, pancreas and lung, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Prostate cancer cell lines are known to be responsive to estrogen and androgen. The protein expression of Gene NO: 20 appears to be influenced by both estrogen and androgen levels. The prostate cancer tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 20 are useful in the intervention and detection of prostate hyperplasia and prostate cancer.

15

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 21**

The translation product of Gene NO: 21 is identical to the human wnt-7a gene. Wnt-7a is a secreted signaling molecule, thought to be important in signaling and the regulation of cell fate and pattern formation during embryogenesis. Specifically, knock out studies in mice have demonstrated that wnt7a plays a critical role in the development of the dorsal-ventral patterning in the developing limb, and to a lesser extent plays a role in the development of anterior-posterior patterning. Overexpression of wnt7a can induce transformation of cultured mammary cells, suggesting that it is an oncogene.

Expression of Gene NO: 21 has only been observed in testes.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, testicular cancer; abnormal limb development. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the testes or developing embryo. For a number of disorders of the above tissues or cells, particularly of the developing embryo, expression of this gene at significantly higher or lower levels may routinely be detected in the developing embryo or amniotic fluid taken from a pregnant individual and compared relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Also, expression of this gene at significantly higher or lower levels may routinely be detected in the testes of patient suffering from testicular cancer and compared relative to the

standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to mouse wnt7a indicates that polypeptides and polynucleotides corresponding to Gene NO: 21 are useful to restore abnormal limb development in an affected individual. Furthermore, its oncogenic potential and tissue distribution indicates that it could serve as a diagnostic for testicular cancer.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 154 as residues: Gly-22 to Arg-28.

10

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 22**

Gene NO: 22 is expressed primarily in fetal liver/spleen, breast, testes and placenta and to a lesser extent in brain, and a series of cancer tissues.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, brain diseases, male infertility, and disposition to pregnant miscarriages. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, hematopoietic system, and sexual organs, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., liver, spleen, testes, placenta, and brain, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene indicates that polypeptides and polynucleotides corresponding to Gene NO: 22 are useful as a marker for non-differentiated, dividing cells and hence could serve as an oncogenic marker. Its high expression in fetal liver, suggests an involvement in hematopoiesis and/or the immune system. Hence it is useful as a factor to enhance an individuals immune system, e.g., in individuals with immune disorders. It is also thought to affect the survival, proliferation, and differentiation of a number of hematopoietic cell lineages, including hematopoietic stem cells. Its disruption, e.g., mutation or altered expression, may also be a marker of immune disorder. Its expression in the testes, suggests it may be important in controlling male fertility. Expression of this gene in breast further reflects a

role in immune function and immune surveillance (breast lymph node). This gene is believed to be useful as a marker for breast cancer.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 155 as residues: Gln-57 to Lys-70 and Ala-91 to Pro-100.

5

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 23**

Gene NO: 23 is expressed primarily in bone marrow and brain (whole and fetal).

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological, immune and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous and hematopoietic systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., bone marrow, brain, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 23 are useful in the diagnosis and treatment of disorders related to the central nervous system (e.g. neuro-degenerative conditions, trauma, and behavior abnormalities) and hematopoiesis. In addition, the expression in fetal brain indicates a role for this gene product in diagnosis of predisposition to developmental defects of the brain.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 156 as residues: Thr-23 to Tyr-29.

30

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 24**

Gene NO: 24 is expressed primarily in smooth muscle, placenta, prostate, and osteoblasts.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular pathologies. Similarly, polypeptides and antibodies

directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular, reproductive and skeletal systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., placenta, smooth muscle, prostate, and osteoblasts, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 24 are useful for detection and treatment of neoplasias and developmental abnormalities associated with these tissues.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 157 as residues: Asn-21 to Thr-26.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 25**

The translation product of Gene NO: 25 shares sequence homology with Pregnancy Associated Mouse Protein (PAMP)-1. (See, FEBS Lett 1993 May 17;322(3):219-222). Based on the sequence similarity the translation product of this gene is expected to share certain biological activities with PAMP-1.

Gene NO: 25 is expressed primarily in 12-week-old human embryos and prostate.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate disorders (cancer). Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., embryonic tissue, and prostate, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.



The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 25 are useful for the diagnosis and treatment of prostate disorders (such as cancer) and developmental abnormalities and fetal deficiencies. The homology to PAMP-1 indicates that this gene and gene product are useful in detecting pregnancy.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 158 as residues: Pro-23 to Glu-28 and Ser-44 to Gly-55.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 26**

Gene NO: 26 is expressed primarily in testes and to a lesser extent in epididymis.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive and endocrine disorders, as well as testicular cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive and endocrine systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., testes, and epididymis, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 26 are useful for the treatment and diagnosis of conditions concerning proper testicular function (e.g., endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to be useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 159 as residues: Pro-24 to Gly-33 and Arg-70 to Gly-76.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 27**

5           The translation product of Gene NO: 27 shares sequence homology with salivary protein precursors which are thought to be important in immune response and production of secreted proteins.

Gene NO: 27 is expressed primarily in salivary gland tissue.

Therefore, polynucleotides or polypeptides of the invention are useful as  
10 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, diseases of the salivary gland. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a  
15 number of disorders of the above tissues or cells, particularly of the immune system, digestive system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., salivary gland, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder,  
20 relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to salivary secreted protein indicates that polypeptides and polynucleotides corresponding to Gene NO: 27 are useful for treatment of immune disorders and diagnostic uses related to secretion of protein in  
25 disease states. For example, the gene product can be used as an anti-microbial agent, an ingredient for oral or dental hygiene, treatment of xerostomia, sialorrhea, intervention for inflammation including parotitis, and an indication for tumors in the salivary gland (adenomas, carcinomas).

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
30 160 as residues: Asp-21 to Gly-28, Asp-30 to Glu-43, Glu-49 to Glu-62, and Thr-75 to Pro-83.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 28**

Gene NO: 28 is expressed primarily in human fetal heart tissue and to a lesser  
35 extent in olfactory tissue.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, olfactory and cardiovascular disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, olfactory and vascular systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., olfactory tissue, and heart, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 28 are useful for diagnosis and treatment of immune, olfactory and vascular disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 161 as residues: Cys-33 to Gly-44, Arg-71 to Arg-78, Ser-130 to Gly-142, Lys-150 to Gly-157, and Thr-159 to Asp-177.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 29**

Gene NO: 29 is expressed primarily in brain and to a lesser degree in activated macrophages, endothelial and smooth muscle cells, and some bone cancers.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of brain and endothelial present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegeneration, inflammation and other immune disorders, fibrotic conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification brain, smooth muscle, and endothelium. For a number of disorders of the above tissues or cells, particularly of the brain and endothelium, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues or cell types (e.g., brain, endothelial cells, macrophages, smooth muscle, and bone, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Tissue distribution suggests polypeptides and polynucleotides corresponding to Gene NO: 29 are useful in study and treatment of neurodegenerative and immune disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 162 as residues: Asn-18 to Glu-20, Ser-33 to Gln-48, Cys-55 to Ser-56, Pro-67 to Cys-69.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 30**

Gene NO: 30 is expressed primarily in early stage human brain and to a lesser extent in cord blood, heart, and some tumors.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of developing CNS tissue present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular and neurodegenerative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and immune systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., brain and heart, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that that polypeptides and polynucleotides corresponding to Gene NO: 30 are useful for the treatment of cancer and of neurodegenerative and cognitive disorders.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 31**

Gene NO: 31 is expressed primarily in brain and thymus and to a lesser extent in several other organs and tissues including the hematopoietic system, liver skin and bone

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, CNS disorders, hematopoietic system disorders, disorders of the endocrine system, bone, and skin. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential

identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly CNS disorders, hematopoietic system disorders, disorders of the endocrine system, bone, and skin, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g.,

5 hematopoietic cells, brain, thymus, liver, bone, and epidermis, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

10 The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 31 are useful for treatment and diagnosis of CNS disorders, hematopoietic system disorders, disorders of the endocrine system, and of bone and skin.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
15 164 as residues: Thr-35 to Arg-40, Pro-55 to His-75, Pro-93 to Ala-98, Ala-111 to Pro-119, and Pro-132 to Glu-138.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 32**

Gene NO: 32 is expressed primarily in organs and tissue of the nervous system  
20 and to a lesser extent in various developing tissues and organs.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the central nervous system and disorders of developing and  
25 growing tissues and organs. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly disorders of the CNS, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., tissue of the nervous  
30 system and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

35 The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 32 are useful for diagnosis and treatment of disorders of the central nervous system, general neurological diseases and neoplasias.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 165 as residues: Ser-33 to Lys-41 and Glu-86 to Glu-91.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 33**

5       Residues 141-156 in the translation product for Gene NO: 33 as shown in the sequence listing matches phosphopantetheine binding site motifs. Phosphopantetheine (or pantetheine 4' phosphate) is the prosthetic group of acyl carrier proteins (ACP) in some multienzyme complexes where it serves as a 'swinging arm' for the attachment of activated fatty acid and amino-acid groups. Phosphopantetheine is attached to a serine  
10       residue in these proteins. ACP proteins or domains have been found in various enzyme systems which are listed below. Fatty acid synthetase (FAS), which catalyzes the formation of long-chain fatty acids from acetyl-CoA, malonyl-CoA and NADPH. Bacterial and plant chloroplast FAS are composed of eight separate subunits which correspond to the different enzymatic activities; ACP is one of these polypeptides.  
15       Fungal FAS consists of two multifunctional proteins, FAS1 and FAS2; the ACP domain is located in the N-terminal section of FAS2. Vertebrate FAS consists of a single multifunctional enzyme; the ACP domain is located between the beta-ketoacyl reductase domain and the C-terminal thioesterase domain. Based on the presence of a phosphopantetheine binding site in the translation product of this gene, it is believed to  
20       share activities fatty acid synthetase polypeptides. Such activities may be assayed by methods known in the art.

This gene is expressed primarily in developing and rapidly growing tissues like placenta fetal heart and endometrial tumor and to a lesser extent in B and T cell lymphoma tissues

25       Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and disorders of developing tissues and organs. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing  
30       immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic tissues and developing organs and tissues, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., embryonic tissue, endometrium, B-cells, and T-cells, and cancerous and wounded  
35       tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to

the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 33 are useful for treatment and diagnosis of cancer in the hematopoietic system developing organs and tissues. It may also be useful for induction of cell growth in disorders of the hematopoietic system and other tissue and organs. The homology to fatty acid synthetases indicates that this gene product is useful in the diagnosis and treatment of lipid metabolism disorders such as hyperlipidemia.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 166 as residues: Arg-27 to Glu-34.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 34**

Gene NO: 34 is expressed primarily in breast and testes tissues and to a lesser extent in hematopoietic tissues including tonsils, T cells and monocytes.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the reproductive organs and systems, including cancer, autoimmune diseases and inflammatory diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive organs and hematopoietic tissues, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., hematopoietic cells, T-cells and monocytes, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Nucleic acids comprising sequence of this gene are also useful as chromosome markers since this gene maps to Chr.15, D15S118-D15S123.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 34 are useful for treatment of diseases of the reproductive organs and hematopoietic system including cancer, autoimmune diseases and inflammatory diseases.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 167 as residues: Phe-81 to Lys-86.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 35**

The translation product of Gene NO: 35 shares sequence similarity with the mouse cytokine-inducible inhibitor of signaling. See, e.g., Nature 1997 Jun 26;387(6636):917-921. Cytokines are secreted proteins that regulate important cellular responses such as proliferation and differentiation. Key events in cytokine signal transduction are well defined: cytokines induce receptor aggregation, leading to activation of members of the JAK family of cytoplasmic tyrosine kinases. In turn, members of the STAT family of transcription factors are phosphorylated, dimerize and increase the transcription of genes with STAT recognition sites in their promoters. Less is known of how cytokine signal transduction is switched off. Expression of the mouse SOCS-1 protein inhibited both interleukin-6- induced receptor phosphorylation and STAT activation. We have also cloned two relatives of SOCS-1, named SOCS-2 and SOCS-3, which together with the previously described CIS form a new family of proteins. Transcription of all four SOCS genes is increased rapidly in response to interleukin-6, in vitro and in vivo, suggesting they may act in a classic negative feedback loop to regulate cytokine signal transduction. The translation product of this gene is believed to have similar biological activities as this family of mouse genes. The biological activity of the translation product of this gene may be assayed by methods shown in Nature 1997 Jun 26;387(6636): 917-921, which is incorporated herein by reference in its entirety.

Gene NO: 35 is expressed primarily in tissues of hematopoietic origin including activated monocytes, neutrophils, activated T-cells and to a lesser extent in breast, adipose tissue and dendritic cells.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the hematopoietic system including cancer autoimmune diseases and inflammatory diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic system expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., hematopoietic cells and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene



expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to cytokine inducible inhibitor of signaling indicates that polypeptides and polynucleotides corresponding to Gene NO: 35 are  
5 useful for diagnosis and treatment of diseases of the hematopoietic system including autoimmune diseases, inflammatory diseases, infectious diseases and neoplasia. For example, administration of, or upregulation of this gene could be used to decrease the response of immune-system to lymphokines and cytokines.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
10 168 as residues: Arg-23 to His-30, Ala-35 to Gly-42.

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 36**

Gene NO: 36 is expressed primarily in infant brain and to a lesser extent in osteoclastoma, placenta, and a wide variety of other tissues.

Therefore, polynucleotides or polypeptides of the invention are useful as  
15 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential  
20 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., osteoclastoma, placenta, and tissue of the central nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial  
25 fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 36 are useful for diagnosis and treatment of neurologic  
30 disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 169 as residues: Gln-31 to Ser-37, Ile-49 to Gly-54, Tyr-57 to Asp-67, Gln-141 to Pro-151, and Val-207 to Thr-219.

### **35 FEATURES OF PROTEIN ENCODED BY GENE NO: 37**

Gene NO: 37 is expressed primarily in osteoclastoma stromal cells, dendritic cells, liver, and placenta.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer, wound, pathological conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues or cell types (e.g., stromal cells, dendritic cells, liver, and placenta and, cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 37 are useful for fundamental role in basic growth and development of human.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 170 as residues: Leu-32 to Thr-37 and Arg-48 to Pro-55.

## **20 FEATURES OF PROTEIN ENCODED BY GENE NO: 38**

The translation product of Gene NO: 38 shares sequence homology with a yeast protein, Lpe10p, which may be involved in mRNA processing. (See Accession Nos. 2104457 and 1079682.) It is likely that an upstream signal sequence exists, other than the predicted sequence described in Table 1. Preferred polypeptide fragments comprise the open reading frame upstream from the predicted signal sequence, as well as polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in skin, and to a lesser extent in embryonic tissues, and fetal liver.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, defects of the skin. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., epidermis, liver, and embryonic tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum,

plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 5           The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 38 are useful for diagnosis and treatment of defects of the skin.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 39**

- 10           Gene NO: 39 is expressed primarily in Amygdala, activated monocytes, testis, and fetal liver. Moreover, this gene is mapped to chromosome 4. Thus, polynucleotides of the present invention can be used in linkage analysis as markers for chromosome 4.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
15   biological sample and for diagnosis of diseases and conditions which include, but are not limited to, defects of the brain, immune system and testis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of  
20   disorders of the above tissues or cells, particularly of the brain, immune system and testis, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., Amygdala, monocytes, testes, and liver and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual  
25   having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

          The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 39 are useful for detecting defects of the brain, immune system and testis because of its abundance in these tissues.

30

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 40**

          The translation product of Gene NO: 40 shares sequence homology with lymphoma 3-encoded protein (bcl-3) which is thought to contribute to leukemogenesis when abnormally expressed.

- 35           This gene is expressed primarily in Human Neutrophils, and to a lesser extent in Human Osteoclastoma Stromal Cells (unamplified), Hepatocellular Tumor, and Human Neutrophils, (Activated).

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, chronic lymphocytic leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., neutrophils, osteoclastoma, and kidney, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to lymphoma 3-encoded protein (bcl-3) indicates that polypeptides and polynucleotides corresponding to Gene NO: 40 are useful for treatment of lymphoma and related cancers.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 41**

Gene NO: 41 is expressed primarily in ovary tumor, and to a lesser extent in endometrial stromal cells and fetal brain.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, ovarian or endometrial cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive system and the developing central nervous system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., ovary, endometrium and brain, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 41 are useful for development of factors involved in ovarian or endometrial and general reproductive organ disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
5 174 as residues: Glu-22 to Trp-31, Asn-84 to Asp-90, and Ser-144 to Asp-151.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 42**

The translation product of Gene 42 has sequence identity with a gene designated PTHrP(B). The PTHrP(B) polypeptide inhibits parathyroid hormone related peptide  
10 (PTHrP) activity.

This gene is expressed primarily in adult testis, and to a lesser extent in pituitary.

Therefore polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
15 biological sample and for diagnosis of male reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive system, expression of this gene at significantly higher or lower levels may routinely be  
20 detected in certain tissues (e.g., testes, and pituitary, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Furthermore, based in part on  
25 sequence identity with PTHrP(B), nucleic acids and polypeptides of the present invention may be used to diagnose or treat such conditions as hypercalcemia, osteoporosis, and disorders related to calcium metabolism.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 42 are useful for treatment of male reproductive disorders,  
30 hypercalcemia, osteoporosis, and other disorders related to calcium metabolism.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 175 as residues: Tyr-81 to Met-86, Gly-103 to Ser-108, Glu-127 to Pro-128, Pro-175 to Ser-180, Glu-196 to Lys-203, Pro-235 to Ser-241, and Ala-249 to Ser-264.

#### **35 FEATURES OF PROTEIN ENCODED BY GENE NO: 43**

The translation product of Gene NO: 43 shares sequence homology with brevican, which is thought to be important as a proteoglycan core protein of the

aggrecan/versican family. The translation product of this gene may also contain a hyaluronan (HA)-binding region domain in frame with, but downstream of, the predicted open reading frame (Barta, et al., Biochem. J. 292:947-949 (1993)). The HA-binding domain, also termed the link domain, is found in proteins of vertebrates that are involved in the assembly of extracellular matrix, cell adhesion, and migration. It is about 100 amino acids in length. The structure has been shown to consist of two alpha helices and two antiparallel beta sheets arranged around a large hydrophobic core similar to that of C-type lectin. This domain typically contains four conserved cysteines involved in two disulfide bonds.

10 This gene is expressed primarily in early stage human brain and to a lesser extent in frontal cortex and epileptic tissues.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of disorders associated with, or observed during, neuronal development. Similarly, polypeptides and antibodies directed to these polypeptides are useful as immunological probes for differential identification of neuronal and associated tissues and cell types. For a number of disorders of the above tissues or cells, particularly for those of the nervous system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., brain and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

25 The tissue distribution and homology to brevican indicates that polypeptides and polynucleotides corresponding to Gene NO: 43 are useful for neuronal regulation and signaling. The uses include directing or inhibiting axonal growth for the treatment of neuro-fibromatosis and in detection of glioses.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 176 as residues: Asp-28 to Arg-33 and Arg-126 to Arg-131.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 44**

Gene NO: 44 is the human homolog of Notch-2 (Accession No. 477495) and mouse EGF repeat transmembrane protein (Accession No. 1336628), both genes are important in differentiation and development of an organism. The EGF repeat transmembrane protein is regulated by insulin like growth factor Type I receptor. These proteins are involved in cell-cell signaling and cell fate determination. Based on

homology, it is likely that this gene products also involved in cell differentiation and development. Although the predicted signal sequence is indicated in Table 1, it is likely that a second signal sequence is located further upstream. Moreover, further translated coding regions are likely found downstream from the disclosed sequence, which can easily be obtained using standard molecular biology techniques. A frameshift occurs somewhere around nucleotide 714, causing a frame shift in amino acid sequence from frame +2 to frame +3. However, using the homology of Notch-2 and EGF repeat transmembrane protein, the complete open reading frame can be elucidated. Preferred polynucleotide fragments comprise nucleotides 146-715, 281-715, and 714-965. Other preferred polypeptide fragments comprise the following EGF-like motifs:

5 CRCASGFTGEDC (SEQ ID NO:260), CTCQVGFTGKEC (SEQ ID NO:261),  
 10 CLNLPGSYQCQC (SEQ ID NO:262), CKCLTGFTGQKC (SEQ ID NO:263), and  
 CQCLQGFTGQYC (SEQ ID NO:264).

Gene NO: 44 is expressed primarily in placenta and to a lesser extent in stromal and immune cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hemophilia and other blood disorders, central nervous system disorders, muscle disorders, and any other disorder resulting from abnormal development. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, hematopoietic and vascular systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., placenta, stromal and immune cells and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to Notch-2 indicates that polypeptides and polynucleotides corresponding to Gene NO: 44 are useful for diagnosing and treating disorders relating to abnormal regulation of cell fate, induction, and differentiation of cells (e.g., cancer), epidermal growth factors, axonal pathfinding, and hematopoiesis.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 177 as residues: Gln-27 to Tyr-32, His-45 to Glu-55, Tyr-61 to Gly-77, Glu-99 to Ser-106, Ser-125 to Cys-131, and Thr-138 to Trp-144.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 45**

The translation product of this gene shares sequence homology with Laminin A which is thought to be important in the binding of epithelial cells to basement membrane and is associated with tumor invasion. Moreover, the translated protein is homologous to the *Drosophila* LAMA gene (Accession No. 1314864), a gene expressed in the first optic ganglion of *Drosophila*. Thus, it is likely that the gene product from this gene is involved in the development of the eye. Nucleotide fragments comprising nucleotides 822-1223, 212-475, 510-731, and 1677-1754 are preferred. Also preferred are the polypeptide fragments encoded by these polynucleotide fragments. It is likely that a frame shift occurs somewhere between nucleotides 475 to 510, shifting the open reading frame from +2 to +3. However, the open reading frame can be clarified using known molecular biology techniques.

This gene is expressed primarily in human testes tumor and to a lesser extent in placenta and activated monocytes.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, invasive cancers or tumors of the epithelium, as well as disorders relating to eye development. Similarly, polypeptides and antibodies directed to these polypeptides are useful as immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of neoplastic conditions, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., testes, placenta, and monocytes and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to Laminin A indicates that polypeptides and polynucleotides corresponding to Gene NO: 45 are useful for study and diagnosis of malignant or benign tumors, fibrotic disorders, and eye disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 178 as residues: Met-1 to Gly-8, Glu-32 to Ala-37, Met-113 to Asn-119, and Glu-139 to Gln-153.



**FEATURES OF PROTEIN ENCODED BY GENE NO: 46**

The translation product of Gene NO: 46 is novel and shares sequence homology with the product of the *Drosophila* tissue polarity gene frizzled. In vertebrates, it appears that there is a family of proteins that represent frizzled gene homologs. (See, e.g., Accession Nos. 1946343 and AFO17989.) The *Drosophila* frizzled protein is thought to transmit polarity signals across the plasma membrane of epidermal cells. The structure of frizzled proteins suggest that they may function as a G-protein-coupled receptor. The frizzled proteins are thought to represent receptors for Wnt gene products - secreted proteins that control tissue differentiation and the development of embryonic and adult structures. Inappropriate expression of Wnts has also been demonstrated to contribute to tumor formation. Moreover, mammalian secreted frizzled related proteins are thought to regulate apoptosis. (See Accession No. AFO17989.) The human homolog has also been recently cloned by other groups. (See Accession No. H2415415.) Thus, the protein encoded by this gene plays a role in mediating tissue differentiation, proliferation, tumorigenesis and apoptosis. Preferred polypeptide fragments lack the signal sequence as described in Table 1, as well as N-terminal and C-terminal deletions. Preferred polynucleotide fragments encode these polypeptide fragments.

Gene NO: 46 is expressed primarily in fetal tissues - particularly fetal lung - and adult cancers, most notably pancreas tumor and Hodgkin's lymphoma. Together, this distribution is consistent with expression in tissues undergoing active proliferation. The gene is also expressed to a lesser extent in other organs, including stomach, prostate, and thymus.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer (particularly pancreatic cancer and/or Hodgkin's lymphoma), as well as other forms of aberrant cell proliferation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and hyperproliferative disorders, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., fetal tissue, pancreas, and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e.,

the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to frizzled indicates that polypeptides and polynucleotides corresponding to Gene NO: 46 are useful for influencing cell proliferation, differentiation, and apoptosis. The full-length protein or a truncated domain could potentially bind to and regulate the function of specific factors, such as Wnt proteins or other apoptotic genes, and thereby inhibit uncontrolled cellular proliferation. Expression of this protein within a cancer - such as via gene therapy or systemic administration - could effect a switch from proliferation to differentiation, thereby arresting the progression of the cancer.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 179 as residues: Pro-31 to Arg-37.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 47**

The translation product of Gene NO: 47 shares sequence homology with members of the Rh/T2/S-glycoprotein family of ribonuclease-encoding genes. These ribonuclease proteins are found predominantly in fungi, plants, and bacteria and have been implicated in a number of functions, including phosphate-starvation response, self-incompatibility, and responses to wounding. A second group has recently cloned this same gene, calling it a ribonuclease 6 precursor. (See Accession No. 2209029.) This group also mapped the gene to chromosome 6, thus, the polynucleotides of the present invention can be used in linkage analysis as a marker for chromosome 6.

Gene NO: 47 is expressed primarily in hematopoietic cells and tissues, including macrophages, eosinophils, CD34 positive cells, T-cells, and spleen. It is also expressed to a lesser extent in brain and spinal cord.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tumors of a hematopoietic origin, graft rejection, wounding, inflammation, and allergy. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., hematopoietic cells, and tissues and cells of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder,

relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to the Rh/T2/S-glycoprotein family of ribonuclease-encoding genes indicates that polypeptides and polynucleotides  
5 corresponding to Gene NO: 47 are useful as a cytotoxin that could be directed against specific cell types (e.g. cancer cells; HIV- infected cells), and that would be well tolerated by the human immune system.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 180 as residues: Ala-24 to Asp-30, Ile-51 to Tyr-61, Pro-69 to Ser-78, Pro-105 to Phe-  
10 110, Asn-129 to Phe-135, Pro-187 to Glu-192, Lys-205 to Gln-224, and Pro-250 to His-256.

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 48**

The translation product of Gene NO: 48 shares sequence homology with  
15 dolichyl-phosphate glucosyltransferase, a transmembrane-bound enzyme of the endoplasmic reticulum which is thought to be important in N-linked glycosylation, by catalyzing the transfer of glucose from UDP-glucose to dolichyl phosphate. (See Accession No. 535141.) Based on homology, it is likely that this gene product also play a role similar in humans. Preferred polynucleotide fragments comprise nucleotides  
20 132-959. Also preferred are the polypeptide fragments encoded by this nucleotide fragment.

Gene NO: 48 is expressed primarily in endothelial cells and to a lesser extent in hematopoietic cells and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as  
25 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, defects in proper N-linked glycosylation of proteins, such as Wiskott-Aldrich syndrome; tumors of an endothelial cell origin. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes  
30 for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular and hematopoietic systems, as well as brain, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., endothelial cells,  
hematopoietic cells, and brain, and cancerous and wounded tissues) or bodily fluids  
35 (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene

expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to dolichyl-phosphate glucosyltransferase indicates that polypeptides and polynucleotides corresponding to Gene NO: 48 are  
5 useful in diagnosing and treating defects in N-linked glycosylation pathways that contribute to disease conditions and/or pathologies.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 181 as residues: Lys-50 to Thr-55, Ser-73 to Arg-79, Glu-92 to Pro-99, Asp-110 to Ser-117, Gln-125 to Lys-131, Gly-179 to Asn-188, Ile-231 to Cys-236, and Glu-318  
10 to Asn-324.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 49**

Gene NO: 49 is expressed primarily in brain, most notably in the hypothalamus and amygdala. This gene is also mapped to chromosome X, and therefore, can be used  
15 in linkage analysis as a marker for chromosome X.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tumors of a brain origin; neurodegenerative disorders, and sex-linked  
20 disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., brain and cancerous and wounded tissues) or bodily  
25 fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides  
30 corresponding to Gene NO: 49 are useful for the diagnosis of tumors of a brain origin, and the treatment of neurodegenerative disorders, such as Parkinson's disease, and sex-linked disorders.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 50**

35 The translation product Gene NO: 50 shares sequence homology with canine phospholemman, a major plasma membrane substrate for cAMP-dependent protein kinases A and C. (See Accession No. M63934; see also Accession No. A40533.) In

fact, a group also recently cloned the human phospholemman gene, and mapped this gene to chromosome 19. (See Accession No.1916010.) Phospholemman is a type I integral membrane protein that gets phosphorylated in response to specific extracellular stimuli such as insulin and adrenalin. Phospholemman forms ion channels in the cell membrane and appears to regulate taurine transport, suggesting an involvement in cell volume regulation. It has been proposed that phospholemman is a member of a superfamily of membrane proteins, characterized by single transmembrane domains, which function in transmembrane ion flux. They are capable of linking signal transduction to the regulation of such cellular processes as the control of cell volume.

Gene No 50 is expressed primarily in fetal liver and to a lesser extent in adult brain and kidney, as well as other organs.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, insulin and/or adrenalin defects; diabetes; aberrant ion channel signaling; defective taurine transport; and defects in cell volume regulation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain and/or immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., liver, brain, and kidney, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to phospholemman indicates that polypeptides and polynucleotides corresponding to Gene NO: 50 are useful for treatment of disorders involving the transport of ions and small molecules, in particular taurine. It could also be beneficial for control of pathologies or diseases wherein aberrancies in the control of cell volume are a distinguishing feature, due to the predicted role for phospholemman in the normal control of cell volume. It also may play a role in disorders involving abnormal circulating levels of insulin and/or adrenalin - along with other active secreted molecules - as revealed by its phosphorylation upon stimulation with insulin or adrenalin

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 183 as residues: Ala-20 to Gln-34, Arg-58 to Thr-79, and Leu-87 to Arg-92.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 52**

Gene NO: 52 is expressed primarily in metastatic melanoma and to a lesser extent in infant brain.

5           Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and cancer metastasis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for  
10 differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., epidermis, and brain, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a  
15 disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 52 are useful for diagnosis and treatment of melanoma.

**20   FEATURES OF PROTEIN ENCODED BY GENE NO: 53**

The translation product of Gene NO: 53 shares sequence homology with mucin which is thought to be important cell surface molecule. It also exhibits sequence identity with a calcium channel blocker of *Agelenopsis aperta*. In particular, with those calcium channel blockers which affect neuronal and muscle cells.

25           Gene NO: 53 is expressed primarily in prostate, endothelial cells, smooth muscle and fetal tissues and to a lesser extent in T cells and placenta.

          Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
30 not limited to, prostate cancer, immune disorders, angina, hypertension, cardiomyopathies, supraventricular arrhythmia, oesophageal achalasia, premature labour, and Raynaud's disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,  
35 particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues or cell types (e.g., prostate, and tissue and cells of the immune system, and cancerous and wounded tissues) or

bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 5           The tissue distribution and homology to mucin indicates that polypeptides and polynucleotides corresponding to Gene NO: 53 are useful as a surface antigen for diagnosis of diseases such as prostate cancer and as tumor vaccine.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 54**

- 10           Gene NO: 54 encodes a polypeptide which exhibits sequence identity with the rab receptor and VAMP-2 receptor proteins. (Martincic, et al., J. Biol. Chem. 272 (1997).)

Gene NO: 54 is expressed primarily in placenta, fetal liver, osteoclastoma and smooth muscle and to a lesser extent in T cell, fetal lung and colon cancer.

- 15           Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers, osteoporosis and immuno-related diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing
- 20           immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, hematopoiesis system and bone system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., placenta, liver, osteoclastoma, smooth muscle, T-cells, and lung, and colon, and
- 25           cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.
- 30           The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 54 are useful for treating cancer, osteoporosis and immuno-disorders.

- Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 187 as residues: Pro-16 to Phe-21, Pro-24 to Arg-35, Arg-92 to Pro-98, Asn-143 to
- 35           Lys-151, and Leu-169 to Ile-176.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 55**

Gene NO: 55 encodes a protein having sequence identity to the rat galanin receptor GALR2.

Gene NO: 55 is expressed primarily in ovarian cancer.

5 Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of ovarian cancer. Similarly, polypeptides and antibodies directed to those polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders  
10 of the above tissues or cells, particularly of the immune system and reproductive system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., ovary, and tissues and cells of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or cell sample  
15 taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. GALR2 antagonists can be used to treat obesity, bulimia, or Alzheimer's disease, while GALR2 agonists can be used to treat anorexia or pain, or to decrease nociception (claimed). Agonists and antagonists can also be used to  
20 treat numerous other disorders, including cognitive disorders, sensory disorders, motion sickness, convulsion/epilepsy, hypertension, diabetes, glaucoma, reproductive disorders, gastric and intestinal ulcers, inflammation, immune disorders, and anxiety.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 55 are useful for diagnosis and treatment of ovarian cancer.

25

**FEATURES OF PROTEIN ENCODED BY GENE NO: 56**

As indicated in Table 1, the predicted signal sequence of Gene NO: 56 relates to an open reading frame that is homologous to the mouse major histocompatibility locus class III. (See Accession No. 2564953.) Any frame shift mutations that alter the correct  
30 open reading frame can easily be clarified using known molecular biology techniques. Moreover, in the opposite orientation, a second translated product is disclosed. This second translation product of this contig is identical in sequence to intracellular protein lysophosphatidic acid acyltransferase. The nucleotide and amino acid sequences of this translated product have since been published by Stamps and colleagues (Biochem, J.  
35 326 (Pt 2), 455-461 (1997)), West and coworkers (DNA Cell Biol. 6, 691-701 (1997)), Rowan (GenBank Accession No. U89336), and Soyombo and Hofmann (GenBank Accession No. AF020544). This gene is thought to enhance cytokine



signaling response in cells. It is likely that a signal peptide is located upstream from this translated product. Preferred polypeptide fragments comprise the amino acid sequence: GLACWLAGVIFIDRKRTGDAISVMSEVAQTLTQDVXVWVFPEGTRNHNGSML PFKRGAFHLAVQAQVPIVPIVMSSYQDFYCKKERRFTSGQCQVRVLPPVPTEGL  
 5 TPDVPALADRVRHSMMLHCF (SEQ ID NO: 265);  
 PSAKYFFKMAFYNGWILFLAVLAIPVCAVRGRNVENMKILRLMLLHIKYLYGI  
 RVEVRGAHHFPPSQPYVVVSNHQSSDLLGMMEVLPGRCVPIAKR (SEQ ID  
 NO:266); TVFREISTD (SEQ ID NO:267); or LWAGSAGWPAG (SEQ ID NO: 268).  
 Also provided are polynucleotide fragments encoding these polypeptide fragments.

10 Gene NO: 56 is expressed primarily in infant adrenal gland, hypothalamus, 7  
 week old embryonic tissue, fetal lung, osteoclastoma stromal cells, and to a lesser  
 extent in a large number of additional tissues.

Therefore, polynucleotides or polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 15 biological sample and for diagnosis of developmental disorders and osteoclastoma.  
 Similarly, polypeptides and antibodies directed to these polypeptides are useful in  
 providing immunological probes for differential identification of the tissue(s) or cell  
 type(s) in which it is highly expressed. For a number of disorders of the above tissues  
 or cells, particularly during development or of the nervous or bone systems, expression  
 20 of this gene at significantly higher or lower levels may routinely be detected in certain  
 tissues and cell types (e.g., adrenal, embryonic tissue, lung, and osteoclastoma stromal  
 cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine,  
 synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or cell  
 sample taken from an individual having such a disorder, relative to the standard gene  
 25 expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
 individual not having the disorder. Further, expression of this protein can be used to  
 alter the fatty acid composition of a given cell or membrane type.

The tissue distribution indicates that polypeptides and polynucleotides  
 corresponding to Gene NO: 56 are useful for diagnosis and treatment of osteoclastoma  
 30 and other bone and non-bone-related cancers, as well as for the diagnosis and treatment  
 of developmental disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:  
 189 as residues: Gly-29 to Gly-36 and Tyr-49 to Tyr-58.

### 35 **FEATURES OF PROTEIN ENCODED BY GENE NO: 57**

The translation product of Gene NO: 57 shares sequence homology with  
 longevity-assurance protein-1. (See Accession No. g1123105.) Preferred

polynucleotide fragments comprise nucleotides 6-125 and 118-432, as well as the polypeptides encoded by these polynucleotides. It is likely that a second signal sequence exists upstream from the predicted signal sequence in Table 1. Moreover, a frame shift likely occurs between nucleotides 118-125, which can be elucidated using standard molecular biology techniques.

Gene NO: 57 is expressed primarily in fetal liver, kidney, brain, thymus, and bone marrow.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological diseases and hyperproliferative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the fetal liver, kidney, brain, thymus, and bone marrow expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., liver, kidney, brain, thymus, and bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to longevity-assurance protein suggest that Gene NO: 57 encodes a protein useful in increasing life span and in replacement therapy for those suffering from immune system disorders or hyperproliferative disorders caused by underexpression or overexpression of this gene.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 190 as residues: Val-29 to Arg-46 and Gly-50 to Gly-56.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 58**

Domains of the Gene NO: 58 product are homologous to porcine surfactant protein-A receptor. (See Accession No. B48516.) The bovine gene binds surfactant protein-A receptor, modulating the secretion of alveolar surfactant. Based on this homology, the gene product encoded by this gene will likely have activity similar to the porcine gene. Preferred polynucleotide fragments comprise nucleotides 887-1039, as well as the polypeptide fragments encoded by this nucleotide fragment.

Gene NO: 58 is expressed primarily in brain and to a lesser extent in endothelial cells.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the central nervous system including dementia, stroke, neurological disorders, respiratory distress, and diseases affecting the endothelium including inflammatory diseases, restenosis, and vascular diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the placenta, liver, endothelial cells, prostate, thymus, and lung, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., brain, and endothelial cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology indicates that polypeptides and polynucleotides corresponding to Gene NO: 58 are useful for the diagnosis and /or treatment of diseases on the central nervous system, such as a factor that promote neuronal survival or protection, in the treatment of inflammatory disorders of the endothelium, or in disorders of the lung. In addition this protein may inhibit or promote angiogenesis and therefore is useful in the treatment of vascular disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 191 as residues: His-66 to Pro-80, Gly-139 to Ser-146 and Ser-262 to Pro-267.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 59**

The translation product of Gene NO: 59 is homologous to the rat hypertension-induced protein which is thought to be important in hypertension, and found expressed mainly in kidneys. (See Accession No. B61209.) Thus, it is likely that this gene product is involved in hypertension in humans. Preferred polypeptide fragments comprise the short chain dehydrogenase/reductase motif SILGIISVPLSIGYCASKHALRGFFNGLR (SEQ ID NO:269), as well as polynucleotides encoding this polypeptide fragment. Also preferred are polynucleotide fragments of 337-639, as well as the polypeptide fragments encoded by this polynucleotide fragment.

Gene NO: 59 is expressed primarily in liver, spleen, lung, brain, and prostate.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular, immunological, and renal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular, renal, and immune, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., liver, spleen, lung, brain, and prostate, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to hypertension-induced protein indicates that polypeptides and polynucleotides corresponding to Gene NO: 59 are useful for treating hypertension.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 192 as residues: Gln-40 to Glu-45, Glu-96 to Glu-102, Asn-256 to Thr-266, and Asp-308 to Asp-317.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 60**

Gene NO: 60 is expressed primarily in activated T-cell and jurkat cell and to a lesser extent in apoptic T-cell and CD34+ cell. It is likely that alternative open reading frames provide the full length amino acid sequence, which can be verified using standard molecular biology techniques.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, T lymphocyte related diseases or hematopoiesis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., T-cells and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard

gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 60 are useful for diagnosis or treatment of immune system disorders.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 61

The translation product of Gene NO: 61, a vacuolar proton-ATPase, shares sequence homology with a *Caenorhabditis elegans* protein which is thought to be important in development. This protein may be a human secretory homologue that may also influence embryo development. Ludwig, J., also recently cloned this gene from chromaffin granules. (See, Accession No. 2584788.) Although Table 1 indicates the predicted signal peptide sequence, the translated product of this gene may in fact start with the upstream methionine, beginning with the amino acid sequence MAYHGLTV (SEQ ID NO:270). Thus, polypeptides comprising this upstream sequence, as well as N-terminus deletions, are also contemplated in the present invention.

Gene NO: 61 is expressed primarily in human placenta, liver, and Hodgkin's Lymphoma and to a lesser extent in bone marrow. Modest levels of expression were also observed in dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hyperproliferative disorders, defects in embryonic development, and diseases or disorders caused by defects in chromaffin granules. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly cancer, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., placenta, liver, lymph tissue, and bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to *Caenorhabditis elegans* indicates that polypeptides and polynucleotides corresponding to Gene NO: 61 are useful for diagnostic or therapeutic modalities for hyperproliferative disorders, embryonic development disorders, and chromaffin granules disorders.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 62**

The translation product of Gene NO: 62 shares sequence homology with the murine LAG3 gene which is thought to be important in the mediation of natural killer cell (NK cell) activity as previously determined by experiments in mice containing null mutations of LAG3. The similarity of this gene to the CD4 receptor may imply that the gene product may be a secreted, soluble receptor and immune mediator.

Gene NO: 62 is expressed primarily in human fetal heart, meningima, and to a lesser extent in tonsils. This gene also is expressed in the breast cancer cell line MDA 36.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, lymphomas, leukemias, breast cancer and any immune system dysfunction, including those dysfunctions which involve natural killer cell activities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system or breast cancer, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., heart, meningima, and tonsils and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to the LAG3 gene (murine) indicates that the polynucleotides and polypeptides corresponding to Gene NO: 62 are useful for diagnostic and/or therapeutic modalities directed at abnormalities or disease states involving defective immune systems, preferably involving natural killer cell activity, as well as breast cancer.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 195 as residues: Pro-10 to Trp-17, Cys-58 to Pro-67, Thr-76 to Glu-85, and Arg-93 to Asn-101.

**35 FEATURES OF PROTEIN ENCODED BY GENE NO: 63**

The translation product of Gene NO: 63 shares sequence homology with a *Caenorhabditis elegans* alpha-collagen gene (Clg), which is thought to be important in

organism development, as well as other collagen genes. Thus, based on sequence homology, polypeptides of this gene are expected to have activity similar to collagen, including involvement in organ development.

Gene NO: 63 is expressed primarily in human B-Cell Lymphoma, and to a lesser extent in human pituitary tissue. This gene has also demonstrated expression in keratinocytes.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, B-Cell Lymphoma, other lymphomas, leukemias, and other cancers, as well as disorders related to development. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., tissue and/or cells of the immune system, and pituitary, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to *Caenorhabditis elegans* alpha-collagen gene indicates that polypeptides and polynucleotides corresponding to Gene NO: 63 are useful for development of diagnostic and/or therapeutic modalities directed at the detection and/or treatment of cancer, specifically B-Cell Lymphomas, leukemias, or diseases related to development.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 196 as residues: Thr-22 to Arg-27 and Ser-29 to Thr-39.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 64**

The translation product of Gene NO: 64 shares sequence homology with human extracellular molecule olfactomedin, which is thought to be important in the maintenance, growth, or differentiation of chemosensory cilia on the apical dendrites of olfactory neurons. Based on this sequence homology, it is likely that polypeptides of this gene have activity similar to the olfactomedin, particularly the differentiation or proliferation of neurons.

Gene NO: 64 is expressed primarily in fetal lung tissue.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the lung as well as neural development, particularly of the lung. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the pulmonary system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., lungs and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to the olfactomedin family indicates that polypeptides and polynucleotides corresponding to Gene NO: 64 are useful for the development of diagnostic and/or therapeutic modalities directed at detection and/or treatment of pulmonary disease states, e.g., cystic fibrosis.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 197 as residues: Gly-17 to Gln-23, Gln-45 to Arg-50, Arg-56 to Lys-61, Glu-70 to Leu-76, Asp-88 to Glu-93, Pro-117 to Met-131, Asp-161 to Glu-167, Arg-224 to Asn-237, Asp-302 to Trp-312, Pro-315 to Asn-320, and Thr-337 to Ser-341.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 65**

The translation product of Gene NO: 65 shares sequence homology with *Saccharomyces cerevisiae* hypothetical protein YKL166 (Accession No. gi/687880) which is thought to be important in secretory and/or vesicular transport mechanisms. Based on this homology, it is likely that the gene product would have similar activity to YKL166, particularly secretory or transport mechanisms. Preferred polypeptide fragments of this gene include those fragments starting with the amino acid sequence ISAARV (SEQ ID NO:271). Other polypeptide fragments include the former fragment, which ends with the amino acid sequence PDVSEFMTRLF (SEQ ID NO:272). Further preferred fragments include those polypeptide fragments comprising the amino acid sequence FDPVRVDITSKGKMRAR (SEQ ID NO:273). Also preferred are polypeptide fragments having exogenous signal sequences fused to the polypeptide.

Gene No 65 is expressed primarily in placenta, testis, osteoclastoma and to a lesser extent in adrenal gland.



Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and/or diseases involving defects in protein secretion. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, cartilage and bone, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., placenta, testis, adrenal gland, and osteoclastoma, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to the yeast YKL1GG protein indicates that polypeptides and polynucleotides corresponding to Gene NO: 65 are useful for the development of therapeutic and/or diagnostic modalities targeted at cancer or secretory anomalies, such as genetically caused secretory diseases.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 198 as residues: Ser-18 to Ser-29 and Lys-53 to Arg-74.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 66**

The translation product of Gene NO: 66 shares sequence homology with the human papilloma virus (HPV) E5 ORF region which is thought to be important as a secreted growth factor. Although this is described as a viral gene product, it is believed to have several cellular secretory homologues. Therefore, based on the sequence similarity between the HPV E5 ORF and the translated product of this gene, this gene product is likely to have activity similar to HPV E5 ORF.

Gene NO: 66 is expressed primarily in activated T-Cells, monocytes, cerebellum and to a lesser extent in infant brain.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and/or human papilloma virus infection. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of

this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., brain, lymph tissue, monocytes, and T-cells and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Moreover, polynucleotides of this gene have been mapped to chromosome 1. Therefore, polynucleotides of the present invention can be used in linkage analysis as a marker for chromosome 1.

The tissue distribution and homology to human papilloma virus E5 region indicates that polypeptides and polynucleotides corresponding to Gene NO: 66 are useful for development of diagnostic and/or therapeutic modalities directed at the diagnosis and/or treatment of cancer and/or human papilloma virus infection (HPV).

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 199 as residues: Asn-31 to Arg-36 and Leu-102 to Ser-112.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 67

The translation product of Gene NO: 67 shares sequence homology with the 8hs20 protein precursor [*Mus musculus*] which is thought to be important in B-Cell mu chain assembly. (See, Accession No. PID/d1002996; Shiraswa, T., EMBO. J. 12(5):1827-1834 (1993).) A polypeptide fragment starting at amino acid 53 is preferred, as well as 1-20 amino acid N-terminus and/or C-terminus deletions. Based on the sequence similarity between 8hs20 protein and the translation product of this gene, the two polypeptides are expected to share certain biological activities, particularly immunologic activities.

Gene NO: 67 is expressed primarily in human B-cells and to a lesser extent in Hodgkin's Lymphoma. It is also likely that the polypeptide will be expressed in B-cell specific cells, bone marrow, and spleen, as is observed with 8hs20.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Hodgkin's Lymphoma, Common Variable Immunodeficiency, and/or other B-cell lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., bone

marrow, spleen, lymph tissue, and B-cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to 8hs20 protein precursor [*Mus musculus*], indicates that polypeptides and polynucleotides corresponding to Gene NO: 67 are useful for therapeutic and/or diagnostic purposes, targeting Hodgkin's Lymphoma, B-cell lymphomas, Common Variable Immunodeficiency, or other immune disorders.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 200 as residues: Asp-51 to Trp-56, Arg-72 to Asp-85, and Gln-106 to Asp-112.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 68**

Gene NO: 68 is expressed primarily in fetal liver/spleen, rhabdomyosarcoma, and to a lesser extent in 9 week-old early stage human embryo and bone marrow.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, rhabdomyosarcoma and other cancers, hematopoietic disorders, and immune dysfunction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues (e.g., embryonic tissue, striated muscle, liver, spleen, and bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that the protein product of Gene NO: 68 is useful for diagnostic and/or therapeutic purposes directed to cancer, preferably rhabdomyosarcoma. Enhanced expression of this gene in fetal liver, spleen, and bone marrow indicates that this gene plays an active role in hematopoiesis. Polypeptides or polynucleotides of the present invention may therefore help modulate survival, proliferation, and/or differentiation of various hematopoietic lineages, including the hematopoietic stem cell. Thus, polynucleotides or polypeptides can be used treat

various hematopoietic disorders and influence the development and differentiation of blood cell lineages, including hematopoietic stem cell expansion. The polypeptide does contain a thioredoxin family active site at amino acids 64-82. Polypeptides comprising this thioredoxin active site are contemplated.

5

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 69**

Gene NO: 69 is expressed primarily in liver and kidney and to a lesser extent in macrophages, uterus, placenta, and testes.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal disorders, neoplasms (e.g., soft tissue cancer, hepatocellular tumors), immune disorders, endocrine imbalances, and reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic, urogenital, immune, and reproductive systems, expression of this gene at significantly higher or lower levels may routinely be detected in certain tissues and cell types (e.g., liver, kidney, uterus, placenta, testes, and macrophages and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 69 are useful for diagnosis and treatment of disorders in the hepatic, urogenital, immune, and reproductive systems.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 202 as residues: Arg-41 to Ser-50, Glu-138 to Asn-148, Ser-155 to Arg-172, Pro-219 to Glu-228.

30

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 70**

Gene NO: 70 is expressed primarily in the immune system, including macrophages, T-cells, and dendritic cells and to a lesser extent in fetal tissue.

Therefore, polynucleotides or polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, inflammatory diseases, lymph node disorders, fetal

35

development, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic systems expression of this gene at  
5 significantly higher or lower levels may routinely be detected in certain tissues and certain cell types (e.g., macrophages, T-cells, dendritic cells, and fetal tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level  
10 in healthy tissue or bodily fluid from an individual not having the disorder. There is some evidence that the polynucleotide is mapped to chromosome 19. Thus, the polynucleotide can be a marker for genetic analysis for chromosome 19.

The tissue distribution indicates that polypeptides and polynucleotides corresponding to Gene NO: 70 are useful for treatment, prophylaxis, and diagnosis of  
15 immune and autoimmune diseases, such as lupus, transplant rejection, allergic reactions, arthritis, asthma, immunodeficiency diseases, leukemia, and AIDS. The polypeptides or polynucleotides of the present invention are also useful in the treatment, prophylaxis, and detection of thymus disorders, such as Graves Disease, lymphocytic thyroiditis, hyperthyroidism, and hypothyroidism. The expression observed  
20 predominantly in hematopoietic cells also indicates that the polynucleotides or polypeptides are important in treating and/or detecting hematopoietic disorders, such as graft versus host reaction, graft versus host disease, transplant rejection, myelogenous leukemia, bone marrow fibrosis, and myeloproliferative disease. The polypeptides or polynucleotides are also useful to enhance or protect proliferation, differentiation, and  
25 functional activation of hematopoietic progenitor cells (e.g., bone marrow cells), useful in treating cancer patients undergoing chemotherapy or patients undergoing bone marrow transplantation. The polypeptides or polynucleotides are also useful to increase the proliferation of peripheral blood leukocytes, which can be used in the combat of a range of hematopoietic disorders, including immunodeficiency diseases, leukemia, and  
30 septicemia.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO: 203 as residues: Thr-21 to Ser-27, Pro-33 to Ser-38, and Arg-73 to Lys-84.

Gene No.	cDNA Clone ID	ATCC Deposit No.: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
1	HGCMD20	97901 02/26/97 209047 05/15/97	pSport1	11	1739	25	1658	54	54	134	1	28	29	466
2	HLDBG33	97898 02/26/97 209044 05/15/97	pCMVSPORT 3.0	12	844	1	844	39	39	135	1	28	29	221
2	HLDBG33	97898 02/26/97 209044 05/15/97	pCMVSPORT 3.0	81	795	1	434	10	10	204	1	29	30	34
3	HTGEW86	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	13	776	134	676	173	173	136	1	35	36	155
4	HKCSR70	97900 02/26/97 209046 05/15/97	pBluescript	14	1376	727	1343	202	202	137	1	20	21	232
4	HKCSR70	97900 02/26/97 209046 05/15/97	pBluescript	82	1324	741	1309		861	205	1	31	32	42

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA OR F
4	HETBI87	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	83	1494	1	1484	51	51	206	1	34	35	84
5	HTEAU17	97897 02/26/97 209043 05/15/97	Uni-ZAP XR	15	502	1	502	143	143	138	1	33	34	60
6	HBMICY91	97897 02/26/97 209043 05/15/97	pBluescript	16	425	1	425	56	56	139	1	17	18	72
7	HSSGE07	97897 02/26/97 209043 05/15/97	Uni-ZAP XR	17	1316	1	1298	45	45	140	1	26	27	376
7	HSSGE07	97897 02/26/97 209043 05/15/97	Uni-ZAP XR	84	1285	1	1271	15	15	207	1	28	29	207
8	HBMBOX59	97897 02/26/97 209043 05/15/97	pBluescript	18	436	87	384	157	157	141	1	21	22	42

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
9	HNGIT22	97897 02/26/97 209043 05/15/97	Uni-ZAP XR	19	503	1	503	23	23	142	1	19	20	40
10	HERAD57	97897 02/26/97 209043 05/15/97	Uni-ZAP XR	20	358	1	358	147	147	143	1	31	32	69
11	HCENJ40	97898 02/26/97 209044 05/15/97	Uni-ZAP XR	21	1926	573	1926	157	157	144	1	30	31	482
11	HCENJ40	97898 02/26/97 209044 05/15/97	Uni-ZAP XR	85	394	1	394	166	166	208	1	20	21	23
11	HCENJ40	97898 02/26/97 209044 05/15/97	Uni-ZAP XR	86	1925	573	1925	157	157	209	1	30	31	482
11	HCENJ40	97898 02/26/97 209044 05/15/97	Uni-ZAP XR	87	1818	30	1298		1137	210	1			12



Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
12	HCSRA90	97898 02/26/97 209044 05/15/97	Uni-ZAP XR	22	1224	64	557	80	80	145	1	30	31	225
13	HBJFC03	97898 02/26/97 209044 05/15/97	Uni-ZAP XR	23	694	1	694	181	181	146	1	39	40	44
13	HBJFC03	97898 02/26/97 209044 05/15/97	Uni-ZAP XR	88	539	1	539	215	215	211	1	18	19	19
14	HSNBL85	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	24	796	405	796	1	1	147	1	30	31	131
14	HSNBL85	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	89	855	300	855	513	513	212	1	37	38	54
15	HTEBY26	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	25	662	205	653	77	77	148	1	30	31	91

68

68

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
15	HTEBY26	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	90	628	198	625		275	213	1	31	32	34
16	HMABH07	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	26	1105	40	1105	88	88	149	1	18	19	164
16	HMABH07	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	91	1053	61	1009	79	79	214	1	22	23	229
17	HSKNY94	97899 02/26/97 209045 05/15/97	pBluescript	27	1017	1	1017	97	97	150	1	30	31	138
17	HSKNY94	97899 02/26/97 209045 05/15/97	pBluescript	93	2492	1	943	100	100	216	1	27	28	126
18	HMCDA67	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	28	391	1	391	169	169	151	1	29	30	57

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
19	HOSFF45	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	29	1139	6	1139	109	109	152	1	44	45	47
19	HOSFF45	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	94	3058	1795	2847	1868	1868	217	1	46	47	46
20	HMJAA51	97899 02/26/97 209045 05/15/97	pSport1	30	465	1	370	47	47	153	1	28	29	41
20	HMJAA51	97899 02/26/97 209045 05/15/97	pSport1	95	1099	664	1000	669	669	218	1	33	34	40
21	HTEBF05	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	31	702	1	702	403	403	154	1	24	25	71
22	HTEAL31	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	32	1142	1	518	49	49	155	1	47	48	105

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
22	HTEAL31	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	96	1580	23	422	32	32	219	1	47	48	104
23	HBMCT32	97899 02/26/97 209045 05/15/97	pBluescript	33	928	1	928	48	48	156	1	27	28	28
23	HBMCT32	97899 02/26/97 209045 05/15/97	pBluescript	97	678	72	593	89	89	220	1	27	28	28
24	HSKXE91	97899 02/26/97 209045 05/15/97	pBluescript	34	773	1	773	39	39	157	1	22	23	52
24	HSKXE91	97899 02/26/97 209045 05/15/97	pBluescript	98	1253	507	1253	507	507	221	1			16
25	HPWTB39	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	35	453	1	453	40	40	158	1	25	26	74

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
26	HILEV12	97899 02/26/97 209045 05/15/97	Uni-ZAP XR	36	459	1	459	25	25	159	1	24	25	80
27	HSPAF93	97900 02/26/97 209046 05/15/97	pSport1	37	509	1	509	1	1	160	1	19	20	138
27	HSPAF93	97900 02/26/97 209046 05/15/97	pSport1	99	447	1	447	7	7	222	1	23	24	137
28	HHFGL62	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	38	598	1	598	1	1	161	1	21	22	177
28	HHFGL62	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	100	611	37	611	17	17	223	1	26	27	49
29	HCE1U14	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	39	454	1	454	1	1	162	1	21	22	71

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
29	HCE1U14	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	101	609	176	609	237	237	224	1			14
30	HEBDA39	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	40	425	1	376	223	223	163	1	18	19	66
31	HTHBA79	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	41	2471	141	2471	213	213	164	1	30	31	154
31	HTHBA79	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	102	1770	47	1721	119	119	225	1	31	32	154
31	HTHBA79	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	103	1832	96	1777	138	138	226	1			9
32	HAGBB70	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	42	2659	1172	2659	119	119	165	1	18	19	103

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
32	HAGBB70	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	104	2237	878	2237	1134	1134	227	1			19
33	HETDG84	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	43	1635	100	1580	299	299	166	1	20	21	80
34	HTEGA81	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	44	780	19	717	10	10	167	1	23	24	92
34	HKGJ40	209236 09/04/97	pSport1	105	1822	1	1023	272	272	228	1	23	24	93
34	HKMLK44	209084 05/29/97	pBluescript	106	1712	1	1669	168	168	229	1	21	22	93
35	HTXAK60	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	45	2378	1337	2378	1437	1437	168	1	30	31	57
35	HTXAK60	97900 02/26/97 209046 05/15/97	Uni-ZAP XR	107	1969	1068	1892	989	989	230	1	23	24	36

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
36	HMHBN40	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	46	1772	69	1772	129	129	169	1	30	31	231
36	HMHBN40	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	108	1734	65	1734	100	100	231	1	29	30	80
37	HFVGS85	97901 02/26/97 209047 05/15/97	pBluescript	47	1107	70	1107	83	83	170	1	30	31	71
38	HERAH81	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	48	805	167	764	167	167	171	1	23	24	64
39	HMSEU04	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	49	1408	131	1258	364	364	172	1	22	23	74
40	HNEDJ57	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	50	1813	1	1184	2	2	173	1	1	2	333



Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
41	HNTME13	97901 02/26/97 209047 05/15/97	pSport1	51	2070	74	2070	142	142	174	1	20	21	195
41	HNTME13	97901 02/26/97 209047 05/15/97	pSport1	109	2003	15	1957	68	68	232	1	22	23	300
42	HSXBI25	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	52	1426	1	1426	158	158	175	1	25	26	264
42	HSXBI25	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	110	1320	80	1311	41	41	233	1	29	30	312
43	HSXCK41	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	53	1720	1	1720	161	161	176	1	22	23	137
43	HSXCK41	97901 02/26/97 209047 05/15/97	Uni-ZAP XR	111	1962	299	1962		566	234	1	33	34	47

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
44	HE8CJ26	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	54	1117	1	1107	218	218	177	1	25	26	178
44	HE8CJ26	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	112	1785	30	1087		225	235	1	23	24	33
45	HTTDS54	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	55	1903	1	1903	119	119	178	1	31	32	154
45	HTTDS54	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	113	1842	1	1832	80	80	236	1	36	37	312
46	HLHDY31	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	56	1869	133	1838	124	124	179	1	24	25	294
46	HLHDY31	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	114	1960	90	1960	165	165	237	1	24	25	295

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
47	HMCBP63	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	57	1259	320	1010	352	352	180	1	26	27	255
48	HEMGE83	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	58	1186	33	557	12	12	181	1	18	19	323
49	HHSDC22	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	59	428	1	304	172	172	182	1	34	35	46
50	HHSDZ57	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	60	501	1	501	40	40	183	1	62	63	92
50	HHSDZ57	97902 02/26/97 209048 05/15/97	Uni-ZAP XR	115	536	73	536	73	73	238	1	22	23	91
52	HMMAB12	97903 02/26/97 209049 05/15/97	pSport1	62	595	1	595	308	308	185	1	29	30	42

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
52	HMMAB12	97903 02/26/97 209049 05/15/97	pSport1	118	453	1	453	198	198	241	1	26	27	27
53	HSKDW02	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	63	1478	40	1436	176	176	186	1	39	40	58
53	HSKDW02	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	119	2016	211	1957	317	317	242	1	25	26	57
54	HETGL41	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	64	2033	1	2033	30	30	187	1	30	31	187
54	HETGL41	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	120	2136	110	2134	296	296	243	1	23	24	122
55	HODAZ50	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	65	440	1	440	1	1	188	1	26	27	145

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
55	HODAZ50	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	121	219	1	219		1	244	1	10	11	72
56	HSDGE59	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	66	3301	349	1478	341	341	189	1	30	31	83
57	HE6ES13	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	67	1535	1	1535	331	331	190	1	26	27	57
57	HE6ES13	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	122	1686	239	1678		367	245	1	27	28	48
58	HSSEP68	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	68	1244	402	1244	57	57	191	1	30	31	310
58	HSSEP68	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	123	1211	1	1211	80	80	246	1	30	31	338

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
58	HSSEP68	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	124	1804	402	1526	501	501	247	1			17
59	HRDEV41	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	69	1292	1	1278	70	70	192	1	28	29	317
59	HRDEV41	97903 02/26/97 209049 05/15/97	Uni-ZAP XR	125	1282	31	1088	70	70	248	1	21	22	338
60	HILCJ01	97903 02/26/97 209049 05/15/97	pBluescript SK-	70	1031	498	1031	536	536	193	1	30	31	52
61	HSATP28	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	71	855	178	855	187	187	194	1	28	29	41
62	HHFGL41	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	72	1274	58	1274	118	118	195	1	42	43	101

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
62	HHFGL41	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	126	1296	88	1237	133	133	249	1	39	40	95
63	HBJEM49	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	73	688	1	688	173	173	196	1	18	19	44
63	HBJEM49	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	127	737	1	737	174	174	250	1	20	21	78
64	HSLDI95	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	74	1890	1	1890	112	112	197	1	21	22	354
64	HSLDI95	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	128	1925	1	1829	87	87	251	1	23	24	353
65	HSREG44	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	75	1133	408	1133	531	531	198	1	18	19	73

Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
66	HTXCT40	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	76	585	1	585	1	1	199	1	69	70	112
66	HTXCT40	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	129	2713	2023	2713	2133	2133	252	1	39	40	108
67	HRGDF73	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	77	577	1	577	51	51	200	1	23	24	122
68	HRDBF52	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	78	2278	1458	1935	25	25	201	1	23	24	314
68	HRDBF52	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	130	1011	479	1011	701	701	253	1	20	21	44
68	HKMND45	97976 04/04/97	pBluescript	131	2278	1	1929	25	25	254	1	27	28	314
69	HPEBD70	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	79	1143	601	1097	95	95	202	1	6	7	235



Gene No.	cDNA Clone ID	ATCC Deposit No: Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	Predicted First AA of Secreted Portion	Last AA of OR F
69	HPEBD70	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	132	1088	535	1043	588	588	255	1	27	28	52
70	HMCAB89	97904 02/26/97 209050 05/15/97	Uni-ZAP XR	80	557	1	557	132	132	203	1	25	26	92

Table 1 summarizes the information corresponding to each "Gene No." described above. The nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the "cDNA clone ID" identified in Table 1 and, in some cases, from additional related DNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X.

The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." Some of the deposits contain multiple different clones corresponding to the same gene. "Vector" refers to the type of vector contained in the cDNA Clone ID.

"Total NT Seq." refers to the total number of nucleotides in the contig identified by "Gene No." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." and the "3' NT of Clone Seq." of SEQ ID NO:X. The nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep."

The translated amino acid sequence, beginning with the methionine, is identified as "AA SEQ ID NO:Y," although other reading frames can also be easily translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

The first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." The predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion." Finally, the amino acid position of SEQ ID NO:Y of the last amino acid in the open reading frame is identified as "Last AA of ORF."

SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to the secreted proteins encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1. The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or the deposited clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are species homologs. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below).

It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

- 5           The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified by the one-step method described in Smith and Johnson, *Gene* 67:31-40 (1988). Polypeptides of the invention also can be purified from natural or recombinant sources
- 10       using antibodies of the invention raised against the secreted protein in methods which are well known in the art.

### **Signal Sequences**

- Methods for predicting whether a protein has a signal sequence, as well as the
- 15       cleavage point for that sequence, are available. For instance, the method of McGeoch, *Virus Res.* 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, *Nucleic Acids Res.* 14:4683-4690 (1986) uses the information
- 20       from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, *supra.*) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

- In the present case, the deduced amino acid sequence of the secreted polypeptide
- 25       was analyzed by a computer program called SignalP (Henrik Nielsen et al., *Protein Engineering* 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results
- 30       shown in Table 1.

- As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., +
- 35       or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely

uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

#### **Polynucleotide and Polypeptide Variants**

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

"Identity" per se has an art-recognized meaning and can be calculated using published techniques. (See, e.g.: (COMPUTATIONAL MOLECULAR BIOLOGY, Lesk, A.M., ed., Oxford University Press, New York, (1988); BIOCOMPUTING: INFORMATICS AND GENOME PROJECTS, Smith, D.W., ed., Academic Press, New York, (1993); COMPUTER ANALYSIS OF SEQUENCE DATA, PART I, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, (1994); SEQUENCE ANALYSIS IN MOLECULAR BIOLOGY, von Heinje, G., Academic Press, (1987); and SEQUENCE ANALYSIS PRIMER, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, (1991).) While there exists a number of methods to measure identity between two polynucleotide or polypeptide sequences, the term "identity" is well known to skilled artisans. (Carillo, H., and Lipton, D., SIAM J Applied Math 48:1073 (1988).) Methods commonly employed to determine identity or similarity between two sequences include, but are not limited to, those disclosed in "Guide to Huge Computers," Martin J. Bishop, ed., Academic Press, San Diego, (1994), and Carillo, H., and Lipton, D., SIAM J Applied Math 48:1073 (1988). Methods for aligning polynucleotides or polypeptides are codified in computer programs, including the GCG program package (Devereux, J., et al., Nucleic Acids Research (1984) 12(1):387 (1984)), BLASTP, BLASTN, FASTA (Atschul, S.F. et al., J. Molec. Biol. 215:403 (1990)), Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, WI 53711 (using the local homology algorithm of Smith and Waterman, Advances in Applied Mathematics 2:482-489 (1981).))

When using any of the sequence alignment programs to determine whether a particular sequence is, for instance, 95% identical to a reference sequence, the parameters are set so that the percentage of identity is calculated over the full length of the reference polynucleotide and that gaps in identity of up to 5% of the total number of nucleotides in the reference polynucleotide are allowed.

A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990).) The term "sequence" includes nucleotide and amino acid sequences. In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB search of a DNA sequence to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, and Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, and Window Size=500 or query sequence length in nucleotide bases, whichever is shorter. Preferred parameters employed to calculate percent identity and similarity of an amino acid alignment are: Matrix=PAM 150, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty=0.05, and Window Size=500 or query sequence length in amino acid residues, whichever is shorter.

As an illustration, a polynucleotide having a nucleotide sequence of at least 95% "identity" to a sequence contained in SEQ ID NO:X or the cDNA contained in the deposited clone, means that the polynucleotide is identical to a sequence contained in SEQ ID NO:X or the cDNA except that the polynucleotide sequence may include up to five point mutations per each 100 nucleotides of the total length (not just within a given 100 nucleotide stretch). In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to SEQ ID NO:X or the deposited clone, up to 5% of the nucleotides in the sequence contained in SEQ ID NO:X or the cDNA can be deleted, inserted, or substituted with other nucleotides. These changes may occur anywhere throughout the polynucleotide.

Further embodiments of the present invention include polynucleotides having at least 85% identity, more preferably at least 90% identity, and most preferably at least 95%, 96%, 97%, 98% or 99% identity to a sequence contained in SEQ ID NO:X or the cDNA contained in the deposited clone. Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the polynucleotides having at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity

will encode a polypeptide identical to an amino acid sequence contained in SEQ ID NO:Y or the expressed protein produced by the deposited clone.

Similarly, by a polypeptide having an amino acid sequence having at least, for example, 95% "identity" to a reference polypeptide, is intended that the amino acid sequence of the polypeptide is identical to the reference polypeptide except that the polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the total length of the reference polypeptide. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a reference amino acid sequence, up to 5% of the amino acid residues in the reference sequence may be deleted or substituted with another amino acid, or a number of amino acids up to 5% of the total amino acid residues in the reference sequence may be inserted into the reference sequence. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

Further embodiments of the present invention include polypeptides having at least 80% identity, more preferably at least 85% identity, more preferably at least 90% identity, and most preferably at least 95%, 96%, 97%, 98% or 99% identity to an amino acid sequence contained in SEQ ID NO:Y or the expressed protein produced by the deposited clone. Preferably, the above polypeptides should exhibit at least one biological activity of the protein.

In a preferred embodiment, polypeptides of the present invention include polypeptides having at least 90% similarity, more preferably at least 95% similarity, and still more preferably at least 96%, 97%, 98%, or 99% similarity to an amino acid sequence contained in SEQ ID NO:Y or the expressed protein produced by the deposited clone.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an

organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level.

Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

5           Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., J. Biol. Chem. 268: 2984-2988  
10           (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

          Moreover, ample evidence demonstrates that variants often retain a biological  
15           activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible  
20           amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

25           Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form  
30           are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

          Thus, the invention further includes polypeptide variants which show  
35           substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make



phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

5 The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid  
10 substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham  
15 and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the  
20 protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues  
25 Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues,  
30 where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino  
35 acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

### **Polynucleotide and Polypeptide Fragments**

10 In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence contained in the deposited clone or shown in SEQ ID NO:X. The short nucleotide fragments are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt in length. A fragment "at least 20 nt in  
15 length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in the deposited clone or the nucleotide sequence shown in SEQ ID NO:X. These nucleotide fragments are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

20 Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments having a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, and 701 to the end of SEQ ID NO:X or the cDNA contained in the deposited clone. In this context "about" includes the particularly  
25 recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity.

In the present invention, a "polypeptide fragment" refers to a short amino acid sequence contained in SEQ ID NO:Y or encoded by the cDNA contained in the  
30 deposited clone. Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments from about amino acid number 1-20, 21-40,  
41-60, 61-80, 81-100, 102-120, 121-140, 141-160, and 161 to the end of the coding  
35 region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about"

includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotide fragments encoding these polypeptide fragments are also preferred.

Also preferred are polypeptide and polynucleotide fragments characterized by structural or functional domains, such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions. Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotide fragments encoding these domains are also contemplated.

Other preferred fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

### **Epitopes & Antibodies**

In the present invention, "epitopes" refer to polypeptide fragments having antigenic or immunogenic activity in an animal, especially in a human. A preferred embodiment of the present invention relates to a polypeptide fragment comprising an epitope, as well as the polynucleotide encoding this fragment. A region of a protein molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response. (See, for instance, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983).)

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

5 In the present invention, antigenic epitopes preferably contain a sequence of at least seven, more preferably at least nine, and most preferably between about 15 to about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe, J. G. et al., Science 219:660-666 (1983).)

10 Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow, M. et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle, F. J. et al., J. Gen. Virol. 66:2347-2354 (1985).) A preferred immunogenic epitope includes the secreted protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if  
15 it is long enough (at least about 25 amino acids), without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting.)

As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is  
20 meant to include intact molecules as well as antibody fragments (such as, for example, Fab and F(ab')<sub>2</sub> fragments) which are capable of specifically binding to protein. Fab and F(ab')<sub>2</sub> fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody. (Wahl et al., J. Nucl. Med. 24:316-325 (1983).) Thus, these fragments are preferred,  
25 as well as the products of a FAB or other immunoglobulin expression library. Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies.

### **Fusion Proteins**

30 Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular  
35 locations based on trafficking signals, the polypeptides of the present invention can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

5        Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the  
10       polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

         Moreover, polypeptides of the present invention, including fragments, and specifically epitopes, can be combined with parts of the constant domain of  
15       immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life in vivo. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP A 394,827; Traunecker et al., Nature 331:84-86  
20       (1988).) Fusion proteins having disulfide-linked dimeric structures (due to the IgG) can also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995).)

         Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion  
25       proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified,  
30       would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol.  
35       Chem. 270:9459-9471 (1995).)

         Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In

preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the claimed invention.

10

### **Vectors, Host Cells, and Protein Production**

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as E. coli, Streptomyces and Salmonella typhimurium cells; fungal cells, such as yeast cells; insect cells such as Drosophila S2 and Spodoptera Sf9 cells; animal cells such as CHO, COS,

293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention, and preferably the secreted form, can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

### Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes  
5 known techniques.

The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each polynucleotide of the present invention  
10 can be used as a chromosome marker.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic  
15 cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can  
20 be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, and preselection by hybridization to construct chromosome specific-cDNA libraries.

Precise chromosomal location of the polynucleotides can also be achieved using  
25 fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to  
30 mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes). Preferred polynucleotides correspond to the noncoding regions of the cDNAs because the coding sequences are more likely conserved within gene families, thus increasing the chance of cross  
35 hybridization during chromosomal mapping.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage



analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) .) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in the polynucleotide and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using polynucleotides of the present invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

In addition to the foregoing, a polynucleotide can be used to control gene expression through triple helix formation or antisense DNA or RNA. Both methods rely on binding of the polynucleotide to DNA or RNA. For these techniques, preferred polynucleotides are usually 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991) ) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques are effective in model systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the

present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute  
5 biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags"  
10 which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an  
15 individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely  
20 small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from  
25 polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the  
30 present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to particular tissue prepared from the sequences of the present  
35 invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers  
5 for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

### Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The  
10 following description should be considered exemplary and utilizes known techniques.

A polypeptide of the present invention can be used to assay protein levels in a biological sample using antibody-based techniques. For example, protein expression in tissues can be studied with classical immunohistological methods. (Jalkanen, M., et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-  
15 3096 (1987).) Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and  
20 technetium (99mTc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying secreted protein levels in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-  
25 radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

30 A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, 131I, 112In, 99mTc), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously, or intraperitoneally) into the mammal. It will be understood in the art that the size of the  
35 subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20

millicuries of  $^{99m}\text{Tc}$ . The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).)

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression of a polypeptide of the present invention in cells or body fluid of an individual; (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a disorder.

Moreover, polypeptides of the present invention can be used to treat disease. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B), to inhibit the activity of a polypeptide (e.g., an oncogene), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease. For example, administration of an antibody directed to a polypeptide of the present invention can bind and reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention could be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

#### **Biological Activities**

The polynucleotides and polypeptides of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules

may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides could be used to treat the associated disease.

### Immune Activity

5           A polypeptide or polynucleotide of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells  
10       from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, a polynucleotide or polypeptide of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

15           A polynucleotide or polypeptide of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. A polypeptide or polynucleotide of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic  
20       cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency  
25       (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

          Moreover, a polypeptide or polynucleotide of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, a polynucleotide or polypeptide of the present invention could be used to treat blood  
30       coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, a polynucleotide or polypeptide of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks  
35       (infarction), strokes, or scarring.

          A polynucleotide or polypeptide of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from

inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation,  
5 differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected by the present invention include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis,  
10 glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune  
15 inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by a polypeptide or polynucleotide of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

20 A polynucleotide or polypeptide of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The  
25 administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, a polypeptide or polynucleotide of the present invention may also be used to modulate inflammation. For example, the polypeptide or polynucleotide may  
30 inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute  
35 rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

### **Hyperproliferative Disorders**

A polypeptide or polynucleotide can be used to treat or detect hyperproliferative disorders, including neoplasms. A polypeptide or polynucleotide of the present invention may inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, a polypeptide or polynucleotide of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but are not limited to neoplasms located in the: abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstrom's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

### **Infectious Disease**

A polypeptide or polynucleotide of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, the polypeptide or polynucleotide of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

- Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of viruses, include, but are not limited to the following DNA and RNA viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus,
- 5 Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza), Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g.,
- 10 Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiolitis, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), meningitis, opportunistic infections (e.g., AIDS),
- 15 pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.
- 20 Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following Gram-Negative and Gram-positive bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae,
- 25 Blastomycosis, Bordetella, Borrelia, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, Enterobacteriaceae (Klebsiella, Salmonella, Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Meningococcal), Pasteurellaceae Infections (e.g., Actinobacillus,
- 30 Hearnophilus, Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, and Staphylococcal. These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease,
- 35 respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis, Chlamydia, Syphilis, Diphtheria,



Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. A polypeptide or polynucleotide of the present invention can be used to treat or detect  
5 any of these symptoms or diseases.

Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following families: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis,  
10 Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas. These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), Malaria, pregnancy complications, and toxoplasmosis. A polypeptide or polynucleotide  
15 of the present invention can be used to treat or detect any of these symptoms or diseases.

Preferably, treatment using a polypeptide or polynucleotide of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide  
20 of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

### **Regeneration**

25 A polynucleotide or polypeptide of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal  
30 disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vascular (including vascular endothelium), nervous, hematopoietic, and  
35 skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, a polynucleotide or polypeptide of the present invention may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. A polynucleotide or polypeptide of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using a polynucleotide or polypeptide of the present invention to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotide or polypeptide of the present invention.

20

### **Chemotaxis**

A polynucleotide or polypeptide of the present invention may have chemotaxis activity. A chemotactic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

A polynucleotide or polypeptide of the present invention may increase chemotactic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotactic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that a polynucleotide or polypeptide of the present invention may inhibit chemotactic activity. These molecules could also be used to treat

disorders. Thus, a polynucleotide or polypeptide of the present invention could be used as an inhibitor of chemotaxis.

### **Binding Activity**

5       A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit (antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or  
10   small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural  
15   receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide, either as a secreted protein or on the cell  
20   membrane. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

25       The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations,  
30   polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

35       Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The

antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

- All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptide from suitably manipulated cells or tissues.

- Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

15

#### Other Activities

- A polypeptide or polynucleotide of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.
- 20 A polypeptide or polynucleotide of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide or polynucleotide of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

- 25 A polypeptide or polynucleotide of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, circadian rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

- 30 A polypeptide or polynucleotide of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.
- 35

**Other Preferred Embodiments**

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Clone Sequence and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Start Codon and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Similarly preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X.

Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which comprises a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the material deposited with the American Type Culture Collection and given the ATCC Deposit Number shown in Table 1 for said cDNA Clone Identifier.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the deposit given the ATCC Deposit Number shown in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of the complete open reading frame sequence encoded by said human cDNA clone.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining

whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for identifying the species, tissue or cell type of a biological sample can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for diagnosing a pathological condition can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1.

Also preferred is a polypeptide, wherein said sequence of contiguous amino acids is included in the amino acid sequence of SEQ ID NO:Y in the range of positions beginning with the residue at about the position of the First Amino Acid of the Secreted Portion and ending with the residue at about the Last Amino Acid of the Open Reading Frame as set forth for SEQ ID NO:Y in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a secreted portion of the secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the



amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at  
5 least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at  
10 least 95% identical to the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is an isolated antibody which binds specifically to a  
15 polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in  
20 the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1;  
25 and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining  
30 whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of  
35 polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an

amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

5           Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

          Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in  
10   said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained  
15   in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

          Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a  
20   sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

          Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample  
25   obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid  
30   sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

          In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

35           Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least

90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a secreted portion of a human secreted protein comprising an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y beginning with the residue at the position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y wherein Y is an integer set forth in Table 1 and said position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y is defined in Table 1; and an amino acid sequence of a secreted portion of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a secreted protein activity, which method comprises administering to such an individual a pharmaceutical composition comprising an amount of an isolated

polypeptide, polynucleotide, or antibody of the claimed invention effective to increase the level of said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

### **Examples**

#### **Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample**

Each cDNA clone in a cited ATCC deposit is contained in a plasmid vector. Table 1 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The table immediately below correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 1 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

	<u>Vector Used to Construct Library</u>	<u>Corresponding Deposited Plasmid</u>
	Lambda Zap	pBluescript (pBS)
20	Uni-Zap XR	pBluescript (pBS)
	Zap Express	pBK
	lafmid BA	plafmid BA
	pSport1	pSport1
	pCMVSPORT 2.0	pCMVSPORT 2.0
25	pCMVSPORT 3.0	pCMVSPORT 3.0
	pCR®2.1	pCR®2.1

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS-. The S and K refers to the orientation of the polylinker to the T7 and T3 primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which

are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from  
5 Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., *Focus* 15:59 (1993).) Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1  
10 Blue. Vector pCR<sup>®</sup>2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the  
15 phage vector sequences identified for the particular clone in Table 1, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited in Table 1 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing  
20 the same ATCC Deposit Number contain at least a plasmid for each cDNA clone identified in Table 1. Typically, each ATCC deposit sample cited in Table 1 comprises a mixture of approximately equal amounts (by weight) of about 50 plasmid DNAs, each containing a different cDNA clone; but such a deposit sample may include plasmids for more or less than 50 cDNA clones, up to about 500 cDNA clones.

25 Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 1. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized  
30 using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with <sup>32</sup>P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, Cold Spring, NY (1982).) The plasmid mixture is transformed into a suitable host, as indicated above (such as  
35 XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above.

The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the SEQ ID NO:X (i.e., within the region of SEQ ID NO:X bounded by the 5' NT and the 3' NT of the clone defined in Table 1) are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25  $\mu$ l of reaction mixture with 0.5  $\mu$ g of the above cDNA template. A convenient reaction mixture is 1.5-5 mM  $MgCl_2$ , 0.01% (w/v) gelatin, 20  $\mu$ M each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., *Nucleic Acids Res.* 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then

be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

- 5           This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that  
10       the 5' end sequence belongs to the desired gene.

**Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide**

- A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR  
15       using primers selected for the cDNA sequence corresponding to SEQ ID NO:X., according to the method described in Example 1. (See also, Sambrook.)

**Example 3: Tissue Distribution of Polypeptide**

- Tissue distribution of mRNA expression of polynucleotides of the present  
20       invention is determined using protocols for Northern blot analysis, described by, among others, Sambrook et al. For example, a cDNA probe produced by the method described in Example 1 is labeled with P<sup>32</sup> using the rediprime™ DNA labeling system (Amersham Life Science), according to manufacturer's instructions. After labeling, the probe is purified using CHROMA SPIN-100™ column (Clontech Laboratories, Inc.),  
25       according to manufacturer's protocol number PT1200-1. The purified labeled probe is then used to examine various human tissues for mRNA expression.

- Multiple Tissue Northern (MTN) blots containing various human tissues (H) or human immune system tissues (IM) (Clontech) are examined with the labeled probe using ExpressHyb™ hybridization solution (Clontech) according to manufacturer's  
30       protocol number PT1190-1. Following hybridization and washing, the blots are mounted and exposed to film at -70°C overnight, and the films developed according to standard procedures.

**Example 4: Chromosomal Mapping of the Polynucleotides**

- 35       An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This

primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on  
5 either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

10 **Example 5: Bacterial Expression of a Polypeptide**

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as  
15 BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp<sup>r</sup>), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site  
20 (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses  
25 the lacI repressor and also confers kanamycin resistance (Kan<sup>r</sup>). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml).  
30 The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.<sup>600</sup>) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.



Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded  
5 onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8,  
10 the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the  
15 protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After  
20 renaturation the proteins are eluted by the addition of 250 mM imidazole. Imidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession  
25 Number XXXXXX.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (*lacIq*). The origin of replication (*oriC*) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made  
30 synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA  
insert is generated according to the PCR protocol described in Example 1, using PCR  
35 primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or

Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

5

**Example 6: Purification of a Polypeptide from an Inclusion Body**

The following alternative method can be used to purify a polypeptide expressed in *E. coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

10        Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50  
15        mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

      The cells are then lysed by passing the solution through a microfluidizer (Microfluidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by  
20        centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

      The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C  
25        overnight to allow further GuHCl extraction.

      Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing  
30        for 12 hours prior to further purification steps.

      To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive

Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

- 5 Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium
- 10 acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant  $A_{280}$  monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.
- 15 The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5  $\mu$ g of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

20

#### **Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System**

- In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong
- 25 polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak *Drosophila* promoter in the
- 30 same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

- Many other baculovirus vectors can be used in place of the vector above, such
- 35 as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription,

translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., *Virology* 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the  
5 AUG initiation codon and the naturally associated leader sequence identified in Table 1, is amplified using the PCR protocol described in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al.,  
10 "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

15 The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("GeneClean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4  
20 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA  
25 sequencing.

Five  $\mu$ g of a plasmid containing the polynucleotide is co-transfected with 1.0  $\mu$ g of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., *Proc. Natl. Acad. Sci. USA* 84:7413-7417 (1987). One  $\mu$ g of  
30 BaculoGold™ virus DNA and 5  $\mu$ g of the plasmid are mixed in a sterile well of a microtiter plate containing 50  $\mu$ l of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10  $\mu$ l Lipofectin plus 90  $\mu$ l Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm  
35 tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate

and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 µCi of <sup>35</sup>S-methionine and 5 µCi <sup>35</sup>S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

#### **Example 8: Expression of a Polypeptide in Mammalian Cells**

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLVI, HIVI and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSPORT 2.0, and pCMVSPORT 3.0. Mammalian host cells that could be used  
5 include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable  
10 marker such as dhfr, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of  
15 interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the  
20 mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the  
25 expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No. 209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the  
30 cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by  
35 procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If the naturally occurring signal sequence is used to produce the

secreted protein, the vector does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

5 The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

10 The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five  $\mu$ g of the expression plasmid pC6 is cotransfected with 0.5  $\mu$ g of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo  
15 contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418.  
20 After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1  $\mu$ M, 2  $\mu$ M, 5  $\mu$ M, 10 mM, 20 mM). The same  
25 procedure is repeated until clones are obtained which grow at a concentration of 100 - 200  $\mu$ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

#### **Example 9: Protein Fusions**

30 The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and  
35 albumin increases the halflife time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the

activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which  
5 outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an  
10 expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated  
15 by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally  
20 occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

GGGATCCGGAGCCCAAATCTTCTGACAAACTCACACATGCCCACCGTGCC  
25 CAGCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCAAAACC  
CAAGGACACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGGT  
GGACGTAAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG  
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAAC  
AGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTG  
30 AATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAACCCCC  
ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT  
GTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCT  
GACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGTGGAGTGGGA  
GAGCAATGGGCAGCCGGAGAACAACACTACAAGACCAGCCTCCCGTGCTGG  
35 ACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCA  
GGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGC



ACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAGTGC  
GACGGCCGCGACTCTAGAGGAT (SEQ ID NO:1)

**Example 10: Production of an Antibody from a Polypeptide**

5           The antibodies of the present invention can be prepared by a variety of methods.  
(See, Current Protocols, Chapter 2.) For example, cells expressing a polypeptide of  
the present invention is administered to an animal to induce the production of sera  
containing polyclonal antibodies. In a preferred method, a preparation of the secreted  
protein is prepared and purified to render it substantially free of natural contaminants.  
10   Such a preparation is then introduced into an animal in order to produce polyclonal  
antisera of greater specific activity.

          In the most preferred method, the antibodies of the present invention are  
monoclonal antibodies (or protein binding fragments thereof). Such monoclonal  
antibodies can be prepared using hybridoma technology. (Köhler et al., Nature  
15   256:495 (1975); Köhler et al., Eur. J. Immunol. 6:511 (1976); Köhler et al., Eur. J.  
Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell  
Hybridomas, Elsevier, N.Y., pp. 563-681 (1981).) In general, such procedures  
involve immunizing an animal (preferably a mouse) with polypeptide or, more  
preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in  
20   any suitable tissue culture medium; however, it is preferable to culture cells in Earle's  
modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at  
about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about  
1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

          The splenocytes of such mice are extracted and fused with a suitable myeloma  
25   cell line. Any suitable myeloma cell line may be employed in accordance with the  
present invention; however, it is preferable to employ the parent myeloma cell line  
(SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are  
selectively maintained in HAT medium, and then cloned by limiting dilution as  
described by Wands et al. (Gastroenterology 80:225-232 (1981).) The hybridoma cells  
30   obtained through such a selection are then assayed to identify clones which secrete  
antibodies capable of binding the polypeptide.

          Alternatively, additional antibodies capable of binding to the polypeptide can be  
produced in a two-step procedure using anti-idiotypic antibodies. Such a method  
makes use of the fact that antibodies are themselves antigens, and therefore, it is  
35   possible to obtain an antibody which binds to a second antibody. In accordance with  
this method, protein specific antibodies are used to immunize an animal, preferably a

mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and  
5 can be used to immunize an animal to induce formation of further protein-specific antibodies.

It will be appreciated that Fab and F(ab')<sub>2</sub> and other fragments of the antibodies of the present invention may be used according to the methods disclosed herein. Such fragments are typically produced by proteolytic cleavage, using enzymes such as papain  
10 (to produce Fab fragments) or pepsin (to produce F(ab')<sub>2</sub> fragments). Alternatively, secreted protein-binding fragments can be produced through the application of recombinant DNA technology or through synthetic chemistry.

For in vivo use of antibodies in humans, it may be preferable to use "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using  
15 genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric antibodies are known in the art. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO  
20 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

#### **Example 11: Production Of Secreted Protein For High-Throughput Screening Assays**

25

The following protocol produces a supernatant containing a polypeptide to be tested. This supernatant can then be used in the Screening Assays described in Examples 13-20.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution  
30 (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The  
35 PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at  $2 \times 10^5$  cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

5           The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in Examples 8 or 9, into an appropriately labeled 96-well round bottom plate. With a  
10       multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

15           Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a 12-channel pipetter with tips on every other channel,  
20       adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37°C for 6 hours.

          While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or CHO-5 media (see below) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock  
25       solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

          The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml appropriate media to each well. Incubate at 37°C for 45 or 72 hours  
30       depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

          On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 13-20.

          It is specifically understood that when activity is obtained in any of the assays  
35       described below using a supernatant, the activity originates from either the polypeptide directly (e.g., as a secreted protein) or by the polypeptide inducing expression of other

proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity in a particular assay.

## 5 *HGS-CHO-5 medium formulation:*

### Inorganic Salts

CaCl <sub>2</sub> (anhyd)	116.6 mg/L
CuSO <sub>4</sub> ·5H <sub>2</sub> O	0.00130
Fe(NO <sub>3</sub> ) <sub>3</sub> ·9H <sub>2</sub> O	0.050
FeSO <sub>4</sub> ·7H <sub>2</sub> O	0.417
KCl	311.80
MgCl <sub>2</sub>	28.64
MgSO <sub>4</sub>	48.84
NaCl	6995.50
NaHCO <sub>3</sub>	2400.0
NaH <sub>2</sub> PO <sub>4</sub> ·H <sub>2</sub> O	62.50
Na <sub>2</sub> HPO <sub>4</sub>	71.02
ZnSO <sub>4</sub> ·7H <sub>2</sub> O	.4320

### Lipids

Arachidonic Acid	.002 mg/L
Cholesterol	1.022
DL-alpha-Tocopherol-Acetate	.070
Linoleic Acid	0.0520
Linolenic Acid	0.010
Myristic Acid	0.010
Oleic Acid	0.010
Palmitric Acid	0.010
Palmitic Acid	0.010
Pluronic F-68	100
Stearic Acid	0.010
Tween 80	2.20

## 10 Carbon Source

D-Glucose	4551 mg/L
-----------	-----------

### Amino Acids

L- Alanine	130.85 mg/ml
L-Arginine-HCL	147.50
L-Asparagine-H <sub>2</sub> O	7.50

L-Aspartic Acid	6.65
L-Cystine-2HCL-H <sub>2</sub> O	29.56
L-Cystine-2HCL	31.29
L-Glutamic Acid	7.35
L-Glutamine	365.0
Glycine	18.75
L-Histidine-HCL-H <sub>2</sub> O	52.48
L-Isoleucine	106.97
L-Leucine	111.45
L-Lysine HCL	163.75
L-Methionine	32.34
L-Phenylalanine	68.48
L-Proline	40.0
L-Serine	26.25
L-Threonine	101.05
L-Tryptophan	19.22
L-Tyrosine-2Na-2H <sub>2</sub> O	91.79
L-Valine	99.65

### Vitamins

Biotin	0.0035 mg/L
D-Ca Pantothenate	3.24
Choline Chloride	11.78
Folic Acid	4.65
i-Inositol	15.60
Niacinamide	3.02
Pyridoxal HCL	3.00
Pyridoxine HCL	0.031
Riboflavin	0.319
Thiamine HCL	3.17
Thymidine	0.365
Vitamin B <sub>12</sub>	0.680

### Other Components

HEPES Buffer	25 mM
Na Hypoxanthine	2.39 mg/L
Lipoic Acid	0.105
Sodium Putrescine-2HCL	0.081
Sodium Pyruvate	55.0
Sodium Selenite	0.0067
Ethanolamine	20uM
Ferric Citrate	0.122
Methyl-B-Cyclodextrin complexed with Linoleic Acid	41.70

Methyl-B-Cyclodextrin complexed with Oleic Acid	33.33
Methyl-B-Cyclodextrin complexed with Retinal Acetate	10

*Adjust osmolarity to 327 mOsm*

### **Example 12: Construction of GAS Reporter Construct**

- 5 One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.
- 10 GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with
- 15 IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

- The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks")
- 20 family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

- The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51
- 25 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a
- 30 WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:2)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

- 5 Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

	<u>Ligand</u>	<u>tyk2</u>	<u>JAKs</u> <u>Jak1</u>	<u>Jak2</u>	<u>Jak3</u>	<u>STATS</u>	<u>GAS(elements) or ISRE</u>
	<u>IFN family</u>						
5	IFN- $\alpha$ /B	+	+	-	-	1,2,3	ISRE
	IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
	IL-10	+	?	?	-	1,3	
	<u>gp130 family</u>						
10	IL-6 (Pleiotrohic)	+	+	+	?	1,3	GAS (IRF1>Lys6>IFP)
	IL-11(Pleiotrohic)	?	+	?	?	1,3	
	OnM(Pleiotrohic)	?	+	+	?	1,3	
	LIF(Pleiotrohic)	?	+	+	?	1,3	
	CNTF(Pleiotrohic)	-/+	+	+	?	1,3	
15	G-CSF(Pleiotrohic)	?	+	?	?	1,3	
	IL-12(Pleiotrohic)	+	-	+	+	1,3	
	<u>g-C family</u>						
20	IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
	IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP >>Ly6)(IgH)
	IL-7 (lymphocytes)	-	+	-	+	5	GAS
	IL-9 (lymphocytes)	-	+	-	+	5	GAS
	IL-13 (lymphocyte)	-	+	?	?	6	GAS
	IL-15	?	+	?	+	5	GAS
25	<u>gp140 family</u>						
	IL-3 (myeloid)	-	-	+	-	5	GAS (IRF1>IFP>>Ly6)
	IL-5 (myeloid)	-	-	+	-	5	GAS
	GM-CSF (myeloid)	-	-	+	-	5	GAS
30	<u>Growth hormone family</u>						
	GH	?	-	+	-	5	
	PRL	?	+/-	+	-	1,3,5	
	EPO	?	-	+	-	5	GAS(B-CAS>IRF1=IFP>>Ly6)
35	<u>Receptor Tyrosine Kinases</u>						
	EGF	?	+	+	-	1,3	GAS (IRF1)
	PDGF	?	+	+	-	1,3	
40	CSF-1	?	+	+	-	1,3	GAS (not IRF1)



To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 13-14, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to

5 bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:  
 5':GCGCCTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCG  
 10 AAATGATTTCCTCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:3)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

15 PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCGAAATG  
 20 ATTTCCTCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCC  
CTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCGCCCATTCTCCGC  
CCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGC  
CTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTT  
TGCAAAAAGCTT:3' (SEQ ID NO:5)

25 With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase,  
 30 alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter  
 35 element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 13-14.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 15 and 16. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

**Example 13: High-Throughput Screening Assay for T-cell Activity.**

The following protocol is used to assess T-cell activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies)

with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

- During the incubation period, count cell concentration, spin down the required number of cells ( $10^7$  per transfection), and resuspend in OPTI-MEM to a final
- 5 concentration of  $10^7$  cells/ml. Then add 1ml of  $1 \times 10^7$  cells in OPTI-MEM to T25 flask and incubate at 37°C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Gentamicin, and 1% Pen-Strep. These cells are treated with supernatants containing a polypeptide as produced by the protocol described in Example 11.

- 10 On the day of treatment with the supernatant, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

- 15 Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100,000 cells per well).

- After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12
- 20 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

- The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples
- 25 from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophane covers) and stored at -20°C until SEAP assays are performed according to Example 17. The plates containing the remaining treated cells are placed at 4°C and serve as a source of material for repeating the assay on a specific well if desired.

- 30 As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

**Example 14: High-Throughput Screening Assay Identifying Myeloid Activity**

The following protocol is used to assess myeloid activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate myeloid cells.

- 5 Myeloid cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

- 10 To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 12, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest  $2 \times 10^7$  U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

- 15 Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM  $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ , 1 mM  $\text{MgCl}_2$ , and 675 uM  $\text{CaCl}_2$ . Incubate at 37°C for 45 min.

- 20 Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37°C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

- 25 These cells are tested by harvesting  $1 \times 10^8$  cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of  $5 \times 10^5$  cells/ml. Plate 200 ul cells per well in the 96-well plate (or  $1 \times 10^5$  cells/well).

- 30 Add 50 ul of the supernatant prepared by the protocol described in Example 11. Incubate at 37°C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 17.

- 35 **Example 15: High-Throughput Screening Assay Identifying Neuronal Activity.**

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat pheochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:6)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:7)

Using the GAS:SEAP/Neo vector produced in Example 12, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 11. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

5        The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as  $5 \times 10^5$  cells/ml.

10        Add 200  $\mu$ l of the cell suspension to each well of 96-well plate (equivalent to  $1 \times 10^5$  cells/well). Add 50  $\mu$ l supernatant produced by Example 11, 37°C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ $\mu$ l of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 17.

15

#### **Example 16: High-Throughput Screening Assay for T-cell Activity**

NF- $\kappa$ B (Nuclear Factor  $\kappa$ B) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by  
20        expression of certain viral gene products. As a transcription factor, NF- $\kappa$ B regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- $\kappa$ B appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

25        In non-stimulated conditions, NF-  $\kappa$ B is retained in the cytoplasm with I- $\kappa$ B (Inhibitor  $\kappa$ B). However, upon stimulation, I-  $\kappa$ B is phosphorylated and degraded, causing NF-  $\kappa$ B to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF-  $\kappa$ B include IL-2, IL-6, GM-CSF, ICAM-1 and class I MHC.

30        Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF- $\kappa$ B promoter element are used to screen the supernatants produced in Example 11. Activators or inhibitors of NF- $\kappa$ B would be useful in treating

diseases. For example, inhibitors of NF- $\kappa$ B could be used to treat those diseases related to the acute or chronic activation of NF- $\kappa$ B, such as rheumatoid arthritis.

To construct a vector containing the NF- $\kappa$ B promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF- $\kappa$ B binding site (GGGGACTTTCCC) (SEQ ID NO:8), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:  
 5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC  
 TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:9)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:  
 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene)  
 Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGGACTTTCC  
 ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCCA  
 TCCCGCCCCTAACTCCGCCCAGTTCGCCCCATTCTCCGCCCCATGGCTGACT  
 AATTTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTC  
 CAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCCTTTTGCAAAAAGCTT:  
 3' (SEQ ID NO:10)

Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF- $\kappa$ B/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF- $\kappa$ B/SV40/SEAP cassette is removed from the above NF- $\kappa$ B/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the NF- $\kappa$ B/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

Once NF- $\kappa$ B/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 13. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described in Example 13. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

#### **Example 17: Assay for SEAP Activity**

As a reporter molecule for the assays described in Examples 13-16, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15  $\mu$ l of 2.5x dilution buffer into Optiplates containing 35  $\mu$ l of a supernatant. Seal the plates with a plastic sealer and incubate at 65°C for 30 min. Separate the Optiplates to avoid uneven heating.

Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50  $\mu$ l Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50  $\mu$ l Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

#### **Reaction Buffer Formulation:**

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6



23	125	6.25
24	130	6.5
25	135	6.75
26	140	7
27	145	7.25
28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

**Example 18: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability**

5 Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a  
10 fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-3, used here.

15 For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO<sub>2</sub> incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-3 is made in 10% pluronic acid DMSO. To load the cells with fluo-3, 50  $\mu$ l of 12  $\mu$ g/ml fluo-3 is added to each well. The plate is incubated at 37°C in a CO<sub>2</sub> incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100  $\mu$ l of buffer.

- 5 For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10<sup>6</sup> cells/ml with HBSS in a 50-ml conical tube. 4  $\mu$ l of 1 mg/ml fluo-3 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37°C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10<sup>6</sup> cells/ml, and dispensed into a microplate, 100  
10  $\mu$ l/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley CellWash with 200  $\mu$ l, followed by an aspiration step to 100  $\mu$ l final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-3. The supernatant is added to the well, and a change in fluorescence is detected.

- To measure the fluorescence of intracellular calcium, the FLIPR is set for the  
15 following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50  $\mu$ l. Increased emission at 530 nm indicates an extracellular signaling event which has resulted in an increase in the intracellular Ca<sup>++</sup> concentration.

20

#### **Example 19: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity**

- The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase  
25 RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

- 30 Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members  
35 of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, the identification of novel human secreted proteins capable of activating tyrosine kinase signal transduction pathways are of interest. Therefore, the following protocol is designed to identify those novel human secreted proteins capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed with PBS and stored at 4°C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 11, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na<sub>3</sub>VO<sub>4</sub>, 2 mM Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub> and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4°C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a

biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

- 5           The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg<sub>2+</sub> (5mM ATP/50mM MgCl<sub>2</sub>), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl<sub>2</sub>, 5 mM MnCl<sub>2</sub>, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the
- 10 components gently and preincubate the reaction mix at 30°C for 2 min. Initiate the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA and place the reactions on ice.

- Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction
- 15 mixture to a microtiter plate (MTP) module and incubating at 37°C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37°C for one hour. Wash the well as
- 20 above.

- Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of
- 25 tyrosine kinase activity.

#### **Example 20: High-Throughput Screening Assay Identifying Phosphorylation Activity**

- As a potential alternative and/or complement to the assay of protein tyrosine
- 30 kinase activity described in Example 19, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase,
- 35 Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other

phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then  
5 rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4°C  
10 until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 11 for 5-20 minutes. The cells are then solubilized and extracts  
15 filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and  
20 Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation.

25

**Example 21: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide**

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from  
30 these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky, D., et al., Science 252:706 (1991).

35 PCR products is then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies).

The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

5 PCR products is cloned into T-tailed vectors as described in Holton, T.A. and Graham, M.W., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals is identified by mutations not present in unaffected individuals.

10 Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenin deoxy-uridine 5'-triphosphate (Boehringer Mannheim), and FISH performed as described in Johnson, Cg. et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

15 Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson, Cv. et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated  
25 disease.

#### **Example 22: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample**

30 A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

35 For example, antibody-sandwich ELISAs are used to detect soluble polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method

described in Example 10. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

#### **Example 23: Formulating a Polypeptide**

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1 µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracisternally, intravaginally,

intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules. Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., *Biopolymers* 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (R. Langer et al., *J. Biomed. Mater. Res.* 15:167-277 (1981), and R. Langer, *Chem. Tech.* 12:98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE 3,218,121; Epstein et al., *Proc. Natl. Acad. Sci. USA* 82:3688-3692 (1985); Hwang et al., *Proc. Natl. Acad. Sci. USA* 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides.

Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.



The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

**Example 24: Method of Treating Decreased Levels of the Polypeptide**

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form.

- 5 Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

- 10 For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 23.

**Example 25: Method of Treating Increased Levels of the Polypeptide**

- 15 Antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

- For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 20 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 23.

**Example 26: Method of Treatment Using Gene Therapy**

- 25 One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is 30 turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin, is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

5 pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

10 The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to  
15 transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is  
20 then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media,  
25 containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is  
30 required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is being produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads,  
35

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

- 5           The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference.

## (1) GENERAL INFORMATION:

(i) APPLICANTS: Human Genome Sciences, Inc. et al.

(ii) TITLE OF INVENTION: 70 Human Secreted Proteins

5 (iii) NUMBER OF SEQUENCES: 273

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Human Genome Sciences, Inc.

(B) STREET: 9410 Key West Avenue

(C) CITY: Rockville

10 (D) STATE: Maryland

(E) COUNTRY: USA

(F) ZIP: 20850

(v) COMPUTER READABLE FORM:

15 (A) MEDIUM TYPE: Diskette, 3.50 inch, 1.4Mb storage

(B) COMPUTER: HP Vectra 486/33

(C) OPERATING SYSTEM: MSDOS version 6.2

(D) SOFTWARE: ASCII Text

(vi) CURRENT APPLICATION DATA:

20 (A) APPLICATION NUMBER:

(B) FILING DATE: March 6, 1998

(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER:

25 (B) FILING DATE:

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: A. Anders Brookes

(B) REGISTRATION NUMBER: 36,373

(C) REFERENCE/DOCKET NUMBER: PS001PCT

## (vi) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: (301) 309-8504

(B) TELEFAX: (301) 309-8439

## 5 (2) INFORMATION FOR SEQ ID NO: 1:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 733 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

10 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

GGGATCCGGA GCCCAAATCT TCTGACAAA CTCACACATG CCCACCGTGC CCAGCACCTG	60
AATTCGAGGG TGCACCGTCA GTCTTCCTCT TCCCCCAA ACCCAAGGAC ACCCTCATGA	120
15 TCTCCCGGAC TCCTGAGGTC ACATGCGTGG TGGTGGACGT AAGCCACGAA GACCCTGAGG	180
TCAAGTTCAA CTGGTACGTG GACGGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGGG	240
AGGAGCAGTA CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT	300
GGCTGAATGG CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGCCCTCCCA ACCCCCATCG	360
AGAAAACCAT CTCCAAGCC AAAGGCAGC CCCGAGAACC ACAGGTGTAC ACCCTGCCCC	420
20 CATCCCGGGA TGAGCTGACC AAGAACCAGG TCAGCCTGAC CTGCCTGGTC AAAGGCTTCT	480
ATCCAAGCGA CATCGCCGTG GAGTGGGAGA GCAATGGGCA GCCGGAGAAC AACTACAAGA	540
CCACGCCTCC CGTGCTGGAC TCCGACGGCT CCTTCTTCCT CTACAGCAAG CTCACCGTGG	600
ACAAGAGCAG GTGGCAGCAG GGGAACGTCT TCTCATGCTC CGTGATGCAT GAGGCTCTGC	660
ACAACCACTA CACGCAGAAG AGCCTCTCCC TGTCTCCGGG TAAATGAGTG CGACGGCCGC	720
25 GACTCTAGAG GAT	733

## (2) INFORMATION FOR SEQ ID NO: 2:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

30 (B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Trp Ser Xaa Trp Ser

5                      1                      5

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 86 base pairs

10 (B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

15 GCGCCTCGAG ATTTCCCCGA AATCTAGATT TCCCCGAAAT GATTTCCCCG AAATGATTTC 60

CCCGAAATAT CTGCCATCTC AATTAG . 86

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 27 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

25 GCGGCAAGCT TTTTGCAAAG CCTAGGC 27

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 271 base pairs

30 (B) TYPE: nucleic acid

162

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CTCGAGATTT CCCCGAAATC TAGATTTCCC CGAAATGATT TCCCCGAAAT GATTTCCCCG 60  
5 AAATATCTGC CATCTCAATT AGTCAGCAAC CATAGTCCCCG CCCCTAACTC CGCCCATCCC 120  
GCCCCTAACT CCGCCCACTT CCGCCCATTC TCCGCCCAT GGCTGACTAA TTTTTTTTAT 180  
TTATGCAGAG GCCGAGGCCG CCTCGGCCTC TGAGCTATTC CAGAAGTAGT GAGGAGGCTT 240  
TTTTGGAGGC CTAGGCTTTT GCAAAAAGCT T 271

10 (2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

GCGCTCGAGG GATGACAGCG ATAGAACCCC GG 32

20 (2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

25 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

GCGAAGCTTC CCGACTCCCC GGATCCGCCT C 31

30 (2) INFORMATION FOR SEQ ID NO: 8:



163

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

5

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

GGGGACTTTC CC

12

## 10 (2) INFORMATION FOR SEQ ID NO: 9:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 73 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

15

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

GCGGCCCTCGA GGGGACTTTC CCGGGGACTT TCCGGGGACT TTCCGGGACT TTCCATCCTG

60

CCATCTCAAT TAG

73

20

## (2) INFORMATION FOR SEQ ID NO: 10:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 256 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

25

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

30 CTCGAGGGGA CTTCCTCCGGG GACTTTCCTGG GGACTTTCCTG GGACTTTCCTCA TCTGCCATCT

60

164

CAATTAGTCA GCAACCATAG TCCCGCCCCCT AACTCCGCCC ATCCCGCCCC TAACTCCGCC 120  
 CAGTTCCGCC CATTCTCCGC CCCATGGCTG ACTAATTTTT TTTATTTATG CAGAGGCCGA 180  
 GGCCGCCTCG GCCTCTGAGC TATTCCAGAA GTAGTGAGGA GGCTTTTTTG GAGGCCTAGG 240  
 CTTTTGCAAA AAGCTT 256

5

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1739 base pairs

(B) TYPE: nucleic acid

10

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

GCGCTCCCGA GGCCGCGGGA CCTGCAGAGA GGACAGCCGG CCTGCGCCGG GACATGCGGC 60  
 15 CCCAGGAGCT CCCAGGCTC GCGTTCCTGT TGCTGCTGTT GCTGTTGCTG CTGCTGCCGC 120  
 CGCCGCCGTG CCTGCCCCAC AGCGCCACGC GTTTCGACCC CACCTGGGAG TCCCTGGACG 180  
 CCCGCCAGCT GCCCGCGTGG TTTGACCAGG CCAAGTTCGG CATCTTCATC CACTGGGGAG 240  
 TGTTTTCCGT GCCCAGCTTC GGTAGCGAGT GGTTCTGGTG GTATTGGCAA AAGGAAAAGA 300  
 TACCGAAGTA TGTGGAATTT ATGAAAGATA ATTACCCTCC TARTTTCAAA TATGAAGATT 360  
 20 TTGGACCACT ATTTACAGCA AAATTTTTTA ATGCCAACCA RTGGGCGARAT ATTTTYCAGG 420  
 CCTCTGGTGC CAAATACATT GTCTTAACTT CCAAACATCA TGAAGGCTTT ACCTTGTTGG 480  
 GGTCAGAATA TTCGTGGAAC TGAATGCCA TAGATGAGGG GCCCAAGAGG GACATTGTCA 540  
 AGGAACTTGA GGTAGCCATT AGGAACAGAA CTGACCTGCG TTTTGGACTG TACTATTCCC 600  
 TTTTGAATG GTTTCATCCG CTCTTCCTTG AGGATGAATC CAGTTCATTC CATAAGCGGC 660  
 25 AATTTCAGT TTCTAAGACA TTGCCAGAGC TCTATGAGTT AGTGAACAAC TATCAGCCTG 720  
 AGGTTCTGTG GTCGGATGGT GACGGAGGAG CACCGGATCA ATACTGGAAC ANCACAGGCT 780  
 TCTTGGCCTG GTTATATAAT GAAAGCCCAG TTCGGGGCAC AGTAGTCACC AATGATCGTT 840  
 GGGGAGCTGG TAGCATCTGT AAGCATGGTG GCTTCTATA CTGCAGTGAT CTTATAACC 900  
 CAGGACATCT TTTGCCACAT AAATGGGAAA ACTGCATGAC AATAGACAAA CTGTCCTGGG 960  
 30 GCTATAGGAG GGAAGCTGGA ATCTCTGACT ATCTTACAAT TGAAGAATTG GTGAAGCAAC 1020

165

TTGTAGAGAC AGTTTCATGT GGAGGAAATC TTTTGATGAA TATTGGGCCC AACTAGATG 1080  
 GCACCATTTTC TGTAGTTTTT GAGGAGCGAC TGAGGCAAAT GGGGTCCTGG CTAAAAGTCA 1140  
 ATGGAGAAGC TATTTATGAA ACCCATACCT GCGGATCCCA GAATGACACT GTCACCCAG 1200  
 ATGTGTGGTA CACATCCAAG CCTAAAGAAA AATTAGTCTA TGCCATTTTT CTAAATGGC 1260  
 5 CCACATCAGG ACAGCTGTTT CTTGGCCATC CCAAAGCTAT TCTGGGGGCA ACAGAGGTGA 1320  
 AACTACTGGG CCATGGACAG CCACTTAACT GGATTTCTTT GGAGCAAAAT GGCATTATGG 1380  
 TAGAACTGCC ACAGCTAACC ATTCATCAGA TGCCGTGTAA ATGGGGCTGG GCTCTAGCCC 1440  
 TRACTAATGT GATCTAAAGT GCAGCAGAGT GGCTGATGCT GCAAGTTATG TCTAAGGCTA 1500  
 GGAAGTATCA GGTGTCTATA ATTGTAGCAC ATGGAGAAAG CAAATGTAAA ACTGGATAAG 1560  
 10 AAAATTATTT TGGCAGTTCA GCCCTTTCCC TTTTCCAC TAAATTTTTT CTAAATTAC 1620  
 CCATGTAACC ATTTTAACTC TCCAGTGCAC TTTGCCATTA AAGTCTCTTC ACATTGAAAA 1680  
 AAAAAAAAAA AAAAACCCCG GGGGGGGG CCGGGNACCC CATTTCGCCC NTAAAGGGG 1739

(2) INFORMATION FOR SEQ ID NO: 12:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 844 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

GGCCCTGGG CCCGAGGGG TGGAGCCGG CCGGGCGAT GTGGAGCGG GGCCGCGGG 60  
 GGGTGCCTG GCCGGTCTG TTGGGGCTG TGCTGGCGT GTTAGTGCCG GCGGTGGTG 120  
 CCGCAAGAC CGGTGCGGAG CTCGTGACCT GCGGGTGGT GCTGAAGCTG CTCAATACG 180  
 ACCACCGCGT GCGGCTGCAC TCGCAGACA TCAAATACG ATCCGGCAGC GGCCAGCAAT 240  
 25 CCGTGACCGG CGTAGAGCG TCGGACGAC CCAATAGCTA CTGGCGGATC CGCGCGGGT 300  
 CGGAGGGCG GTGCCCGGC GGGTCCCCG TCGCTGCGG GCAGGCGGTG AGGCTCACG 360  
 ATGTGCTTAC GGGCAAGAAC CTGCACAGC ACCACTTCCC GTGCGCGCTG TCCAACAACC 420  
 AGGAGGTGAG TGCTTTGGG GAAGACGGG AGGGCGACSA CCTGGACCTA TGGACAGTG 480  
 GCTGCTCTG ACAGCACTG GAGCGTGAG CTGCTGTGG CTTCCAGCAT GTGGGCACCT 540  
 30 CTGTGTTCT GTCACTACG GGTGAGCAGT ATGGAAGCCC CATCCGTGG CAGCATGAG 600

166

TCCACGGCAT GCCCAGTGCC AACACGCACA ATACGTGGAA GGCCATGGAA GGCATCTTCA 660  
 TCAAGCCTAG TGTGGAGCCC TCTGCAGGTC ACGATGAACT CTGAGTGTGT GGATGGATGG 720  
 GTGGATGGAG GGTGGCAGGT GGGGCGTCTG CAGGGCCACT CTGGCAGAG ACTTTGGGTT 780  
 TGTAGGGGTC CTCAAGTGCC TTTGTGATTA AAGAATGTTG GTCTATGAAA AAAAAAAAAA 840  
 5 AAAAA 844

## (2) INFORMATION FOR SEQ ID NO: 13:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 776 base pairs  
 10 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

TTCGAAATAA AAGATCTGCT CAAGAGAGCC GCAGAAAAAG AAGGTGTATG TTGGGGGTTT 60  
 15 AGAGAGCAGG GTCTTGAAAT ACACAGCCCA GAATATGGAG CTCAGAACA AAGTACAGCT 120  
 TCTGGAGGAA CAGAAATTGT CCCTTCTAGA TCÁACTGAGG AACTCCAGG CCATGGTGAT 180  
 TGAGATATCA AACAAAACCA GCAGCAGCAG CACCTGCATC TTGGTCCTAC TAGTCTCCTT 240  
 CTGCCTCCTC CTTGTACCTG CTATGTACTC CTCTGACACA AGGGGAGGCC TGCCAGCTGA 300  
 GCATGGAGTG TTGTCCCGCC AGCTTCGTGC CCTCCCCAGT GAGGACCCTT ACCAGCTGGA 360  
 20 GCTGCCTGCC CTGCAGTCAG AAGTGCCGAA AGACAGCACA CACCAGTGGT TGGACGGCTC 420  
 AGACTGTGTA CTCCAGGCCC CTGGCAACAC TTCCTGCCTG CTGCATTACA TGCTCAGGC 480  
 TCCAGTGCA GAGCCTCCCC TGGAGTGGCC ATTCCCTGAC CTCTTCTCAG AGCCTCTCTG 540  
 CCGAGGTCCC ATCCTCCCCC TGCAGGCAAA TCTACAAGG AAGGGAGGAT GGCTTCCTAC 600  
 25 TGGTAGCCCC TCTGTCATTT TGCAGGACAG ATACTCAGGC TAGATATGAG GATATGTGGG 660  
 GGGTCTCAGC AGGAGCCTGG GGGGCTCCCC ATCTGTGTCC AAATAAAAAG CGGTGGGCAA 720  
 GGGCTGGCCG CAGCTCCTGT GCCCTGTCAE GACGACTGAG GGCTCAAACA CACCAC 776

## (2) INFORMATION FOR SEQ ID NO: 14:

- 30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1376 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

	GAATTCGGCA CGAGGCGCCT ACCCTGCCTG CAGGTGAGCA GTGGTGTGTG AGAGCCAGGC	60
	GTCCCTCTGC CTGCCACTC AGTGGCAACA CCCGGGAGCT GTTTTGTCTT TTGTGGAGCC	120
	TCAGCAGTTC CCTCTTTCAG AACTCACTGC CAAGAGCCCT GAACAGGAGC CACCATGCG	180
	TGCTTCAGCT TCATTAAGAC CATGATGATC CTCTTCAATT TGCTCATCTT TCTGTGTGGT	240
10	GCAGCCCTGT TGGCAGTGGG CATCTGGGTG TCAATCGATG GGCATCCTT TCTGAAGATC	300
	TTGCGGCCAC TGTCGTCCAG TGCCATGCG TTTGTCAACG TGGGCTACTT CCTCATCGCA	360
	GCCGGCGTTG TGGTCTTTGC TCTTGGTTTC CTGGGCTGCT ATGGTGCTAA GACTGAGAGC	420
	AAGTGTGCCC TCGTGACGTT CTTCTTCATC CTCCTCCTCA TCTTCATTGC TGAGGTTGCA	480
	GCTGCTGTGG TCGCCTTGST GTACACCACA ATGGCTGAGC ACTTCCTGAC GTTGCTGGTA	540
15	GTGCCTGCCA TCAAGAAAGA TTATGGTTCC CAGGAAGACT TCACTCAAGT GTGGAACACC	600
	ACCATGAAAG GGTCAAGTG CTGTGGCTTC ACCAACTATA CGGATTTTGA GGAATCACCC	660
	TACTTCAAAG AGAACAGTGC CTTTCCCCCA TTCTGTTGCA ATGACAACGT CACCAACACA	720
	GCCAATGAAA CCTGCACCAA GCAAAAGGCT CACGACCAA AAGTAGAGGG TTGCTTCAAT	780
	CAGCTTTTGT ATGACATCCG AACTAATGCA GTCACCGTGG GTGGTGTGGC AGCTGGAATT	840
20	GGGGGCCTCG AGCTGGCTGC CATGATTGTG TCCATGTATC TGTAAGTCAA TCTACAATAA	900
	GTCCACTTCT GCCTCTGCCA CTAAGTCTGC CACATGGGAA CTGTGAAGAG GCACCTGGC	960
	AAGCAGCAGT GATTGGGGGA GGGGACAGGA TCTAACAATG TCACTTGGGC CAGAATGGAC	1020
	CTGCCCTTTC TGCTCCAGAC TTGGGGCTAG ATAGGGACCA CTCCTTTTAN GCGATGCCTG	1080
	ACTTTCCTTC CATTGGTGGG TGGATGGGTG GGGGGCATTC CAGAGCCTCT AAGGTAGCCA	1140
25	GTCTGTGTC CCATTCCCCC AGTCTATTAA ACCCTTGATA TGCCCCCTAG GCCTAGTGGT	1200
	GATCCCAGTG CTCTACTGGG GGATGAGAGA AAGGCATTTT ATAGCCTGGG CATAAGTGAA	1260
	ATCAGCAGAG CCTCTGGGTG GATGTGTAGA AGGCATTCA AAATGCATAA ACCTGTTACA	1320
	ATGTTTAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAYTCG AGGGGGGTCC CGTACC	1376

30

(2) INFORMATION FOR SEQ ID NO: 15:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 502 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

5

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

	TAAACAGTG CCTGCCTCAA AGGGAGGACT CAGTCAATAT CTGTTGAATG AATGAATGAA	60
	TAATTGCCTG GGTCAACGAA TGAATGGCTG AATGAATGAT TTCTCCTTTC CCTCGGCACT	120
	GTCTGGAGTC CCCAGGACAG GCATGGGCAG CAGTCGCTGG TCTGTGGCCT GTCCCACTGG	180
10	ACTTGGGGTT CTCATGCTTG GTCTGGGCGG AGATCACCCA CCAGGCTCCC AGGTCGATCC	240
	TCTGCTCATG GGAARCTGCG TCCGGCCNA GCTGCCAGAA CTCACTGCAS GGTGGAGGGA	300
	ARARCAGGRA CGATCTGCGA GCGCCTGAAC AGCGCACAAG AGCCGAGGAG CCGCTGCTTA	360
	AAATGCAGGC GTTGAGAGGA GTTTCGCCTC CTTTTTGTAG TTGAATATGA GATTTCCGAG	420
	CAGCCATGAC GAGTTGGGTT GGTGGAAGTG GGGAGTCCGT TCCTCAGTCA GATGGAGGAG	480
15	GGGGTCCCCT TGGATCTCCT CT	502

## (2) INFORMATION FOR SEQ ID NO: 16:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 425 base pairs

20

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

	ATCTCTAGTG GTGGCTGCCG TCGCTCCAGA CAATCGGAAT CCTGCCTTCA CCACCATGGG	60
25	CTGGCTTTTT CTAAAGGTTT TGTGGCGGG AGTGAGTTTC TCAGGATTTT TTTATCCTCT	120
	TGTGGATTTT TGCATCAGTG GGAAACAAG AGGACAGAAG CCAAACCTTG TGATTATTTT	180
	GGCCGATGAC ATGGGGTGGG GTGACTGGGG AGCAAACCTG GCAGAAACAA AGGACACTGC	240
	CAACCTTGAT AAGATGGCTT CGGAGGGAAT GARGTGARTC TTGARATGCC ARGCCAGCTT	300
	TCTTTGGAWG TCTTACTCCC GTTCTTGAAA AGGGAAAGGG GCGTGCAAAG CACTTAARGA	360
30	WTCATKGATG GACCCATGTG ATTTARTTAA TTTATTAATT AATTTGGTTT GGAARCCAGC	420

ATAGC

425

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1316 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

10	GGCACGAGGA GCTGGGGGAG CCTGAGGTGC GCTACGTGGC TGGCATGCAT GGAACGAGG	60
	CCCTGGGGCG GGAGTTGCTT CTGCTCCTGA TGCAGTTCCT GTGCCATGAG TTCCTGCGAG	120
	GGAACCCACG GGTGACCCGG CTGCTCTCTG AGATGCGCAT TCACCTGCTG CCCTCCATGA	180
	ACCTTGATGG CTATGAGATC GCCTACCACC GGGGTTCAGA GCTGGTGGGC TGGGCCGAGG	240
	GCCGCTGGAA CAACCAGAGC ATCGATCTTA ACCATAATTT TGCTGACCTC AACACACCAC	300
15	TGTGGGAAGC ACAGGACGAT GGGAAGGTGC CCCACATCGT CCCCACCAT CACCTGCCAT	360
	TGCCCCACTTA CTACACCCTG CCCAATGCCA CCGTGGCTCC TGAAACGCGG GCAGTAATCA	420
	AGTGGATGAA GCGGATCCCC TTTGTGCTAA GTGCCAACCT CCACGGGGGT GAGCTCGTGG	480
	TGTCCTACCC ATTCGACATG ACTCGCACCC CGTGGGCTGC CCGCGAGCTC ACGCCACAC	540
	CAGATGATGC TGTGTTTCGC TGGCTCAGCA CTGTCTATGC TGGCAGTAAT CTGGCCATGC	600
20	AGGACACCAG CCGCCGACCC TGCCACAGCC AGGACTTCTC CGTGCACGGC AACATCATCA	660
	ACGGGGCTGA CTGGCACACG GTCCCCGGA GCATGAATGA CTTGAGCTAC CTACACACCA	720
	ACTGCTTTGA GGTCACTGTG GAGCTGTCCT GTGACAAGTT CCCTCACGAG AATGAATTGC	780
	CCCAGGAGTG GGAGAACAAC AAAGACGCCC TCCTCACCTA CCTGGAGCAG GTGCGCATGG	840
	GCATTGCAGG AGTGGTGAGG GACAAGGACA CGGAGCTTGG GATTGCTGAC GCTGTGATGC	900
25	CCGTGGATGG GATTAACCAT GACGTGACCA CGGCGTGGGG CGGGGATTAT TGGCGTCTGC	960
	TGACCCACAG GGAATACATG GTGACTGCCA GTGCCGAGGG CTACCATTCA GTGACACGGA	1020
	ACTGTGGGGT CACCTTTGAA GAGGGCCCT TCCCCTGCAA TTTCGTGCTC ACTAAGACTC	1080
	CCAAACAGAG GCTGCGCGAG CTGCTGGCAG CTGGGGCCAA GTGCCCCCG GACCTTCGCA	1140
	GGCCCTTGA GCGGCTAAGG GGACAGAAGG ATTGATACCT GCGGTTTAAG AGCCCTAGGG	1200
30	CAGGCTGGAC CTGTCAAGAC GGGAAGGGGA AGAGTAGAGA GGGAGGGACA AAGTGAGGAA	1260

AAGGTGCTCA TTAAAGCTAC CGGGCACCTT AAAAAAAAAA AAAAAAAAAA AAAAAA

1316

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 436 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

10 AAAAAAATTC AATGGATATT ATGAAAATAA GAGAGTATTT CCAGAAGTAT GGATATAGTC 60  
CACGTGTCAA GAAAAATTCA GTACACGAGC AAGAAGCCAT TAACTCTGAC CCAGAGTTGT 120  
CTAATTGTGA AAATTTTCAG AAGACTGATG TGAAAGATGA TCTGTCTGAT CCTCCTGTTG 180  
CAAGCAGTTG TATTTCTGAG AAGTCTCCAC GTAGTCCACA ACTTTCAGAT TTTGGACTTG 240  
AGCGGTACAT CGTATCCCAA GTTCTACCAA ACCCTCCACA GGCAGTGAAC AACTATAAGG 300  
15 AAGAGCCCGT AATTGTAACC CCACCTACCA AACAATCACT AGTAAAAGTA CTAAAACTC 360  
CAAAATGTGC ACTAAATGG ATGATTTTGA GTGTGTACTC CTAAATTAGA AACTTTGGT 420  
ATCTCTGAAT ATACTA 436

(2) INFORMATION FOR SEQ ID NO: 19:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 503 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

TGTGCATATC CTGGGAAAA AAATGGTACA TGTTTTAGAA ATTTTACTGT TTATAACAAT 60  
GCAGGCAGTC AGTTTCCCGT TTCAAACACA GATAGATACA TTCAACACTC AAGATCCTGC 120  
AGAGAGGCAG CCAGCATCTA TTGTTTAAAA AGGTTTCAAA AAGAATTCGG ATTGCTCKTT 180  
TCTCTTTTGA ATCTGTGTGC CAAATGACAG GGACCAATAT TCGTCTTCTT TTTCKGTAAA 240  
30 AYTCAAGAAAG AMACATGAAA GAACCCAGAA TGCATTTCTT AAAGGGATTT AGTGCAGTTA 300



TTTTAAATAA TTTATGCACG CACACACACA TACATATATC CCCCAGAGTAC ATATTTTTTTC 360  
 CCTTTTACT TGTGTGCAAT CAGTAGCTAC AATGACTGAA ATCCACTTCT TTGGGACTGT 420  
 GACATTTAAG CAAATCTTGT NTCTAGAAAN CGAAATGCCA NANTCTCGCA CAAAGCTGCT 480  
 CCGTCTGGGG CAACAAATCC ACA 503

5

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 358 base pairs

(B) TYPE: nucleic acid

10

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

GGGCTGTCTC CCCAGTAGTA ACTTGCTGGC CCTGCCCTTG AAGTGGGGAA ACTGTGAAGG 60  
 GTCCTTGAT CAAGCTTGTC CTCTTTCTT ACCTCTTCCT CTCTTCTGTT TCCGCTGCAG 120  
 15 CTGAACAGGC CAGCAGGCAA CCTGCCATGG GGTCTGCTC CAAGAACCGG TCCTTCTTCT 180  
 GGATGACTGG GTCCTGGTA TTCATCAGCC TCCTCTCAG TGAGTGGCAG GGTCCCTGGG 240  
 AAGGGAGGGC AATTGGAGAG GGCTGGGCTA GCTGGGCTCT GACCAACGGG TGGGCTGTTC 300  
 AACTTCTGAT GTCTTTGGGC AACAACACAG AAAAACACTC TGTTATGATT TACGAAAN 358

20

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1926 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

25

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

AGTGAAGGGA GCTGGCCGTG CGACTGGGCT TCGGGCCCTG TGCCAGAGGA GCANGCCTTC 60  
 CTGAGCAGGA GGAAGCAGGT GGTGGCCGCG GCCTTGAGGC AGGCCCTGCA GCTGGATGGA 120  
 GACCTGCAGG AGGATGAGAT CCCAGTGGTA GCTATTATGG CCACTGGTGG TGGGATCCGG 180  
 30 GCAATGACTT CCCTGTATGG GCAGCTGGCT GGCCTGAAGG AGCTGGGCCT CTGGATGTC 240

	KTCTCCTACA TCACCGGGGC CTCGGGCTCC ACCTGGGCCT TGGCCAACCT TTATAAGGAC	300
	CCAGAGTGGT CTCAGAAGGA CCTGGCAGGG CCCACTGAGT TGCTGAAGAC CCAGGTGACC	360
	AAGAACAAGC TGGGTGTGCT GGCCCCCAGC CAGCTGCAGC GGTACCGGCA GGAGCTGGCC	420
	GAGCGTGCCC GCTTGGGCTA CCCAAGCTGC TTCACCAACC TGTGGGCCCT CATCAACGAG	480
5	GCGCTGCTGC ATGATGAGCC CCATGATCAC AAGCTCTCAG ATCAACGGGA GGCCCTGAGT	540
	CATGGCCAGA ACCCTCTGCC CATCTACTGT GCCCTCAACA CCAAAGGGCA GAGCCTGACC	600
	ACTTTTGAAT TTGGGGAGTG GTGCGAGTTC TCTCCCTACG AGGTGGGCTT CCCCAAGTAC	660
	GGGGCCTTCA TCCCCTCTGA GCTCTTTGGC TCCGAGTTCT TTATGGGGCA GCTGATGAAG	720
	AGGCTTCCTG AGTCCCGCAT CTGCTTCTTA GAAGGTATCT GGAGCAACCT GTATGCAGCC	780
10	AACTCCAGG ACAGCTTATA CTGGGCCTCA GAGCCCAGCC AGTTCTGGGA CCGCTGGGTC	840
	AGGAACCAGG CCAACCTGGA CAAGGAGCAG GTCCCCCTTC TGAAGATAGA AGAACCACCC	900
	TCAACAGCCG GCAGAATAGC TGAGTTTTC ACCGATCTTC TGACGTGGCG TCCACTGGCC	960
	CAGGCCACAC ATAATTTCTT CCGTGGCCTC CATTTCCACA AAGACTACTT TCAGCATCCT	1020
	CACTTCTCCA CATGGAAAGC TACCACTCTG GATGGGCTCC CCAACCAGCT GACACCCTCG	1080
15	GAGCCCCACC TGTGCCTGCT GGATGTTGGC TACCTCATCA ATACCAGCTG CCTGCCCCTC	1140
	CTGCAGCCCA CTCGGGACGT GGACCTCATC CTGTCAATTG ACTACAACCT CCACGGAGCC	1200
	TTCCAGCAGT TGCAGCTCCT GGGCCGGTTC TGCCAGGAGC AGGGGATCCC GTTCCCACCC	1260
	ATCTCGCCCA GCCCCGAAGA GCAGCTCCAG CCTCGGGAGT GCCACACCTT CTCCGACCCC	1320
	ACCTGCCCCG GAGCCCCTGC GGTGCTGCAC TTTCTCTGG TCAGCGACTC CTTCCGGGAG	1380
20	TACTCGGCCC CTGGGGTCCG GCGGACACCC GAGGAGGCGG CAGCTGGGGA GGTGAACCTG	1440
	TCTTCATCGG ACTCTCCCTA CCACTACAG AAGGTGACCT ACAGCCAGGA GGACGTGGAC	1500
	AAGCTGCTGC ACCTGACACA TTACAATGTC TGCAACAACC AGGAGCAGCT GCTGGAGGCT	1560
	CTGCGCCAGG CAGTGCAGCG GAGGCGGCAG CGCAGGCCCC ACTGATGGCC GGGGCCCTG	1620
	CCACCCCTAA CTCCTATTCA TTCCCTGGCT GCTGAGTTGC AGGTGGGAAC TGTATCACG	1680
25	CAGTGCTTNC AGAGCCTCGG GCTCAGGTGG CACTGTCCCA GGTCCAGGC TGAGGGCTGG	1740
	GAGCTCCCTT GCGCTCAGC AGTTTGAGT GGGGTAAGGA GGCCAAGCCC ATTTGTGTAA	1800
30	TCACCCAAAA CCCCCCGGCC TGTGCCTGTT TTCCCTTCTG CGCTACCTTG AGTAGTTGGA	1860
	GCACTTGATA CATCACAGAC TCATACAAAT GTGAGGCGCT GAGAAAAAAA AAAAAAAAAA	1920
	ACTCGA	1926

(2) INFORMATION FOR SEQ ID NO: 22:

5

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 1224 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

15 CCGCCGAAGC TCCGTCCCGC CCGCGGCCGG CTCCGCCTCA CCTCCCGGCC GCGGCTGCCC 60  
TCTGCCCGGG TTGTCCAAGA TGGAGGGCGC TCCACCGGGG TCGCTCGCCC TCCGGCTCCT 120  
GCTGTTCTGT GCGCTACCGG CCTCCGGCTG GCTGACGACG GGCGCCCCCG AGCCGCCGCC 180  
20 GCTGTCCGGA GCCCCACAGG ACGGCATCAG AATTAATGTA ACTACACTGA AAGATGATGG 240  
GGACATATCT AAACAGCAGG TTGTTCTTAA CATAACCTAT GAGAGTGGAC AGGTGTATGT 300  
AAATGACTTA CTGTAAATA GTGGTGTAA CCGAATAAGC TGTCAGACTT TGATAGTGAA 360  
25 GAATGAAAAT CTGAAAATT TGGAGGAAAA AGAATATTTT GGAATTGTCA GTGTAAGGAT 420  
TTTAGTTCAT GAGTGGCCTA TGACATCTGG TTCCAGTTTG CAACTAATTG TCATTCAAGA 480  
30 AGAGGTAGTA GAGATTGATG GAAAACAAGT TCAGCAAAAG GATGTCACCTG AAATTGATAT 540  
TTTAGTTAAG AACCGGGGAG TACTCAGACA TTCAAATAT ACCCTCCCTT TGAAGAAAG 600  
CATGCTCTAC TCTATTTCTC GAGACAGTGA CATTTTATTT ACCCTTCCTA ACCTCTCCAA 660  
35 AAAAGAAAGT GTTAGTTCAC TGCAAACCAC TAGCCAGTAT CTTATCAGGA ATGTGGAAAC 720  
CACTGTAGAT GAAGATGTTT TACCTGGGCA AGTTACCTGA AACTCCTCTC AGAGCAGAGC 780  
40 CGCCATCTTC ATATAAGGTA ATGTGTCAGT GGATGGAAAA GTTTAGAAAA GATCTGTGTA 840  
GGTCTGGAG CAACGTTTTC CCACTATTCT TTCAGTTTTT GAACATCATG GTGGTTGGAA 900  
TTACAGGAGC AGCTGTGGTA ATAACCATCT TAAAGGTGTT TTTCCAGTT TCTGAATACA 960  
45 AAGGAATTCT TCAGTTGGAT AAAGTGGACG TCATACCTGT GACAGCTATC AACTTATATC 1020  
CAGATGGTCC AGAGAAAAGA GCTGAAAACC TTGAAGATAA AACATGTATT TAAAACGCCA 1080  
50 TCTCATATCA TGGACTCCGA AGTAGCCTGT TGCCTCCAAA TTTGCCACTT GAATATAATT 1140  
TCTTTTAAAT CGTTAAGAAT CAGTTTATAC ACTAGAGAAA TTGCTAAACT CTAAGACTGC 1200  
CTGAAAATTG ACCTTTACAG TGCC 1224  
55

## (2) INFORMATION FOR SEQ ID NO: 23:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 694 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

10 GGCACGAGTC TTATTGTGCA CTGTAGCCTG AATCCCCCAG GGTAATTAAT ATGAAGTGCA 60  
 AAAAGTTGAA TGTTCAGTC TAAAGGCAG TGGGAGAAAT TACATAGCAT GGAAATAATA 120  
 15 AAATGAAGTC TTATTAATGA GAACGAGGCT CTTGCAGTGG CAAGTTCTGC TGGTCACCCG 180  
 ATGGGGATGG GAGCCTTTCA AGCTTTTTTT TGGGTAATAC TCACAGTTTC CAACGCTGTG 240  
 GTACTTTTCA AAATGAGCTT GTTCTTCCTT CTGACACTCA TCTCAAAGCT CCATGGTGAC 300  
 20 GCAGAGGTCT GTTGAAGGTC ACAGGTCTTC GCTTGATTG GCATACGGTC CTGTAGCATC 360  
 ACTTGTTAGC CCACTGCTGC TTGAAGGAAC TAAGAGTATT CAGGGATAGA GAGCTGAAAA 420  
 25 TAGGATTAAT TCCTTCCTTT TGAAGTCTCC CTCAAGATGT CCTTGCTTTG GTCTGAAAAC 480  
 CTCTCCTGAC AACTTTTGCC CAAAGCAAAC CATCTGCCTT TTCTGAACTC TGAGTGAATA 540  
 TATTAGCATC TTCCTTCTG AGCCCTCGTA CTGCCANGTT TGTTTGTTTG TTTGTTTCCA 600  
 30 AGAGACTGTG TCTTGCTCTG TCACCCAGGA GTTTGAAACC AGCCTGGCAA CATAGCAAGA 660  
 CCCTATCTCT ACAAAAAAAA AAAAAAAA AAAA 694

35

## (2) INFORMATION FOR SEQ ID NO: 24:

## (i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 796 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

45

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

ATGAGCGGCG GTTGATGGC GCAGGTGGA GCGTGGCGAA CAGGGGCTCT GGGCCTGGCG 60  
 50 CTGCTGCTGC TGCTCGGCCT CGGACTAGGC CTGGAGGCGC CGCGAGCCCG CTTTCCACCC 120  
 CGACCTCTGC CCAGGCCGCA CCCGAGCTCA GGCTCGTGCC CACCCACCAA GTTCCAGTGC 180  
 CGCACCAGTG GCTTATGCGT GCCCCTCACC TGGCGCTGCG ACAGGACTTG GACTGCAGCG 240  
 55 ATGGCAGCGA TGAGGAGGAG TGCAGGATG AGCCATGTAC CCAGAAAGGG CAATGCCAC 300  
 CGCCCCCTGG CCTCCCTGCG CCCTGCACCG GCGTCAGTGA CTGCTCTGGG GGAAGTACA 360  
 60 AGAAACTGCG CAACTGCAGC CGCCTGGCCT GCCTAGCAGS GRAGSKCMCG WKGACAGCTG 420

175

5  
10  
15

ACGGATGACT GCATTCCACT CACGTGGCGC TCGGACGGCC ACCCAGACTG TCCCAGACTCC 480  
AGCGACGAGC TCGGCTGTGG AACCAATGAG ATCCTCCCGG AAGGGGATGC CACAACCATG 540  
GGGCCCCCTG TGACCCTGGA GAGTGTCAAC TCTCTCAGGA ATGCCACAAC CATGGGGCCC 600  
CCTGTGACCC TGGAGAGTGT CCCCTCTGTC GGAATGCCA CATCCTCCTC TGCCGGAGAC 660  
CAGTCTGGAA GCCCAACTGC CTATGGGGTT ATTGCAGCTG CTGCGGTGCT CAGTGCAAGC 720  
CTGGTCACCG CCACCCTCCT CCTTTTGTCC TGGCTCCGAG CCCAGGAGCG CCTCCGCCCA 780  
CTGGGGTTAC TGGTGG 796

20 (2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 662 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
25 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

30  
35  
40  
45  
50

TAATTCGGCA CGAGGCTGTG GTGGAGAAGG ACGTGCCGTG CCGCTGGGTT CTGAGCCGGA 60  
GTGGTCGGTG GGTGGGATGG AGGCGACCTT GGAGCAGCAC TTGGAAGACA CAATGAAGAA 120  
TCCCTCCATT GTTGGAGTCC TGTGCACAGA TTCACAAGGA CTTAATCTGG GTTGCCCGCG 180  
GACCCTGTCA GATGAGCATG CTGGAGTGAT ATCTGTTCTA GCCCAGCAAG CAGCTAAGCT 240  
AACCTCTGAC CCCACTGATA TTCCTGTGGT GTGTCTAGAA TCAGATAATG GGAACATTAT 300  
GATCCAGAAA CACGATGGCA TCACGGTGGC AGTGCACAAA ATGGCCTCTT GATGCTCATA 360  
TCTGTTCTTC AGCAGCCTGT CATAGGAACT GGATCCTACC TATGTTAATT ACCTTATAGA 420  
ACTACTAAAG TTCCAGTAGT TAGGCCATTC ATTTAATGTG CATTAGGCAC TTTTCTGTTT 480  
ATTTAAGAGT CAATTGCTTT CTAATGCTCT ATGGACCGAC TATCAAGATA TTAGTAAGAA 540  
AGGATCATGT TTTGAAGCAG CAGGTCCAGG TCACTTTGTA TATAGAATTT TGCTGTATTC 600  
AATAAATCTG TTTGGAGGAA AAAAAAAAAA AAAAAAATTA CTGCGGNCCG ACAAGGGAAT 660  
TC 662

55 (2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 1105 base pairs  
60 (B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

5 CCTGATCCTC TCTTTTCTGC AGTTCAAGGG AAAGACGAGA TCTTGCACAA GGCACCTCTGC 60  
 TTCTGCCCTT GGCTGGGGAA GGGTGGCATG GAGCCTCTCC GGCTGCTCAT CTTACTCTTT 120  
 10 GTCACAGAGC TGTCCGAGC CCACAACACC ACAGTGTTC AGGGCGTGGC GGGCCAGTCC 180  
 CTGCAGGTGT CTTGCCCTTA TGAATCCATG AAGCACTGGG GGAGGCGCAA GGCCTGGTGC 240  
 15 CGCCAGCTGG GAGAGAAGGG CCCATGCCAG CGTGTGGTCA GCACGCACAA CTTGTGGCTG 300  
 CTGTCTTCC TGAGGAGGTG GAATGGGAGC ACAGCCATCA CAGACGATAC CCTGGGTGGC 360  
 ACTCTACCA TTACGCTGCG GAATCTACAA CCCCATGATG CGGGTCTCTA CCAGTGCCAG 420  
 20 AGCCTCCATG GCAGTGAGGC TGACACCTC AGGAAGGTCC TGGTGGAGGT GCTCGCAGAC 480  
 CCCCTGGATC ACCGGGATGC TGGAGATCTC TGGTTCCCCG GGGAGTCTGA GAGCTTCGAG 540  
 GATGCCCATG TGGAGCACAG CATCTCCAGG AGCTCTTCKT AGGAAAGGCC GCAAATTCCT 600  
 25 ATTCTTCCC CTCTTGCTTA TCYTTCTCCT CCAAGAYCTG CATCTTTCTC ATCAAGATTC 660  
 TAGCAGCCAG CGCCTCTGG GCTGCAGCCT GGCATGGACA GAAGCCAGGG ACACATCCAC 720  
 30 CCAGTGAACCT GGAATGTGGC CATGACCCAG GGTATCAGCT CCAAACCTG CCAGGGCTGA 780  
 GAGACACGTG AAGGAAGATG ATGGGAGGAA AAGCCCAGGA GAAGTCCAC CAGGGACCAG 840  
 CCCAGCCTGC ATACTTGCCA CTTGGCCACC AGGACTCCTT GTTCTGCTCT GGCAAGAGAC 900  
 35 TACTCTGCCT GAACACTGCT TCTCCTGGAC CCTGGAAGCA GGGACTGGTT GAGGGAGTGG 960  
 GGAGGTGTA AGAACACCTG ACAACTTCTG AATATTGGAC ATTTTAAACA CTTACAAATA 1020  
 40 AATCCAAGAC TGTATATTT AAAAAAAAAA AAAAAAAMA AAARRRRRRC CCCGGTACCC 1080  
 AATCGCCCT ATAGTGAGTC GTATA 1105

45

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 1017 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

CTCGCTGGG CTGTTTCCCG GCTTCATTTT TCCCGACTCA GCTTCCACCC CTGGGCTTTC 60  
 CGAGGTGCTT TCGCCGCTGT CCCCACTACT GCAGCCATGA TCTCTTAAC GGACACGCAG 120  
 60

AAAATTGGAA TGGGATTAAC AGGATTTGGA GTGTTTTTCC TGTCTTTTGG AATGATTCTC 180  
 TTTTTTGACA AAGCACTACT GGCTATTGGA AATGTTTTAT TTGTAGCCGG CTTGGCTTTT 240  
 5 GTAATTGGTT TAGAAAGAAC ATTCAGATTC TTCTTCCAAA AACATAAAAT GAAAGCTACA 300  
 GGTTTTTTC TGGGTGGTGT ATTTGTAGTC CTTATTGGTT GGCCTTTGAT AGGCATGATC 360  
 10 TTCGAAATTT ATGGATTTTT TCTCTGTTC AGGGGCTTCT TTCCTGTCGT TGTGGCTTT 420  
 ATTAGAAGAG TGCCAGTCCT TGGATCCCTC CTAAATTTAC CTGGAATTAG ATCATTTGTA 480  
 GATAAAGTIG GAGAAAGCAA CAATATGGTA TAACAACAAG TGAATTTGAA GACTCATTTA 540  
 15 AAATATTGTG TTATTTATAA AGTCATTIGA AGAATATTCA GCACAAAATT AAATTACATG 600  
 AAATAGCTTG TAATGTTCTT TACAGGAGTT TAAAACGTAT AGCCTACAAA GTACCAGCAG 660  
 CAAATTAGCA AAGAAGCAGT GAAAACAGC TTCTACTCAA GTGAACTAAG AAGAAGTCAG 720  
 20 CAAGCAAAC GAGAGAGGTG AAATCCATGT TAATGATGCT TAAGAACTC TTGAAGGCTA 780  
 TTTGTGTTGT TTTTCCACAA TGTGCGAAAC TCAGCCATCC TTAGAGAACT GTGGTGCCTG 840  
 25 TTTCTTTTCT TTTTATTTTG AAGGCTCAGG AGCATCCATA GGCATTGCT TTTTAGAAAT 900  
 GTCCACTGCA ATGGCAAAAA TATTTCCAGT TGCCTGTAT CTCGGAAGT GATGCATGAA 960  
 TCGATTGGA TTGTGTCATT TTAAAGTATT AAAACCAAGG GAAACCCCAA AAAAAA 1017  
 30

## (2) INFORMATION FOR SEQ ID NO: 28:

35

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 391 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

40

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

CCCTGGAAG AGGAACTGAT GTTTGAGGGG ACAGATGTGG GTCACCTTCC CTGGCAGTGC 60  
 45 CCTCTAGCCT TGCTGCCTTG GCTTTCTGAC CCCTTCCAGG CTTCAGGGGC CTGGGAGATC 120  
 TCATGCCTCA GCCCAGGAAA CATTTAATAG GGAAAGCAGA GACATGTCAT GTCAGCCCCA 180  
 50 CAGACAAGAA TTTCTAGAGC ACTTGTCTTG TTGTTCCCTG CCCCGACATT ACTCAGTCTG 240  
 GGCCATGGAA TCCATCCAAT AAACACAGCA ACACCCTATG NTACTGACCA AGCAAAGCTT 300  
 GCCCCTGGTA CCAAAGAGCT AAATCATGAC CAAAGTGTGA CATGAATGTA ACTGAAATGC 360  
 55 GGGTTAGTTG CTCAATGTAT GCAAAGTCCC A 391

60

## (2) INFORMATION FOR SEQ ID NO: 29:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1139 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

10 GGTGATATCT TCATAGTGGG CTATTACAGG CAGGAAAATG TTTTAACTGG TTTACAAAAT 60  
CCATCAATAC TTGTGTCATT CCCTGTAAAA GGCAGGAGAC ATGTGATTAT GATCAGGAAA 120  
15 CTGCACAAAA TTATTGTTTT CAGCCCCCGT GTTATGTGCC TTTTGAACGT TTTTTTTTTT 180  
ATTAAAGCCA AATTTGTGTT GTATATATTC GTATTCCATG TGTTAGATGG AAGCATTTCC 240  
TATCCAGTGT GAATAAAAAG AACACTTGTA GTAAATTATT ATAAAGCCGA TGATATTTCA 300  
20 TGGCAGGTTA TTCTACCAAG CTGTGCTTGT TGGTTTTTCC CATGACTGTA TTGCTTTTAT 360  
AAATGTACAA ATAGTTACTG AAATGACGAG ACCCTTGTTT GCACAGCATT AATAAGAACC 420  
25 TTGATAAGAA CCATATTCTG TTGACAGCCA GCTCACAGTT TCTTGCCTGA AGCTTGGTGC 480  
ACCCTCCAGT GAGACACAAG ATCTCTCTTT TACCAAAGTT GAGAACAGAG CTGGTGGATT 540  
AATTAATAGT CTTGATATC TGGCCATGGG TAACCTCATT GTAACATCA TCAGAATGGG 600  
30 CAGAGATGAT CTGAAGTGT CACATACACT AAAGTCCAAA CACTATGTCA GATGGGGGTA 660  
AAATCCATTA AAGAACAGGA AAAAATAATT ATAAGATGAT AAGCAAATGT TTCAGCCCAA 720  
35 TGTAACCCA GTTAAAAAAA AAATTAATGC TGTGTAAAT GGTGAATTA GTTTGCAAAC 780  
TATATAAGA CATATGCAGT AAAAAGTCTG TTAATGCACA TCCTGTGGGA ATGGAGTGT 840  
CTAACCAATT GCCTTTTCTT GTTATCTGAG CTCTCTATA TTATCATACT CAGATAACCA 900  
40 AATTAAAAGA ATTAGAATAT GATTTTAAAT ACACTTAACA TTAACTCTT CTAACCTTCT 960  
TCTTCTGTG ATAATTGAGA AGATAGTTAT GGATCTTCAA TGCCTCTGAG TCATTGTTAT 1020  
45 AAAAAATCAG TTATCACTAT ACCATGCTAT AGGAGACTGG GCAAAACCTG TACAATGACA 1080  
ACCCTGGAAG TTGCTTTTTT TAAAAAATA ATAAATTCT TAAATCAAAA AAAAAAAA 1139

50

## (2) INFORMATION FOR SEQ ID NO: 30:

## (i) SEQUENCE CHARACTERISTICS:

- 55 (A) LENGTH: 465 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

60

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:



CCACGCGTCC GCGGACGCGT GGGGAAGGTT TGTGCCAGTA GACATTATGT TACTAAATCA 60  
 GCACTTTAAA ATCTTTGGTT CTCTAATTCA TATGAATTTG CTGTTTGCTC TAATTTCTTT 120  
 5 GGGCTCTTCT AATTTGAGTG GAGTACAATT TTGTGTGAA ACAGTCCAGT GAAACTGTGC 180  
 AGGGAAATGA AGGTAGAATT TTGGGAGGTA ATAATGATGT GAAACATAAA GATTTAATAA 240  
 10 TTACTGTCCA ACACAGTGA GCAGCTTGTC CACAAATATA GTAATTACTA TTTATTGCTC 300  
 TAAGGAAGAT TAAAAAAGA TAGGGAAAAG GGGGAACTT CTTTGAAAAA TGAACATCT 360  
 GTTACATTAA TGTCTAATTA TAAATTTTA ATCCTTACTG CATTTCTTCT GTTCCTACAA 420  
 15 ATGTATTAAA CATTCACTTT AACTGGTAAA AAAAAAAAAA AAAAA 465

20

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

25

- (A) LENGTH: 702 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

30

GCAACAAGCG GCCACCTTC CTGAAGATCA AGAAGCCACT GTCGTACCGC AAGCCCATGG 60  
 ACACGGACCT GGTGTACATC GAGAAGTCGC CCAACTACTG CGAGGAGGAC CCGGTGACCG 120  
 35 GCAGTGTGGG CACCCAGGGC CGCGCCTGCA ACAAGACGGC TCCCCAGGCC AGCGGCTGTG 180  
 ACCTCATGTG CTGTGGGCGT GGCTACAACA CCCACCACTA CGCCCGCGTG TGGCAGTGCA 240  
 ACTGTAAGTT CCACTGGTGC TGCTATGTCA AGTGCAACAC GTGCAGCGAG CGCACGGAG 300  
 40 ATGTACACGT GCAAGTGAGC CCCGTGTGCA CACCACCCTC CCGCTGCAAG TCAGATTGCT 360  
 GGGAGGACTG GACCGTTTCC AAGCTGCGGG CTCCCTGGCA GGATGCTGAG CTTGTCTTTT 420  
 45 CTGCTGAGGA GGGTACTTTT CCTGGGTTTC CTGCAGGCAT CCGTGGGGGA AAAAAAATCT 480  
 CTCAGAGNCC TCAACTATTC TGTTCCACAC CCAATGCTGS TCCACCCTCC CCCAGACACA 540  
 GCCCAGGTCC CTCCGCGGCT GGAGCGAAGC CTCTGCAGC AGGAACTCTG GACCCCTGGG 600  
 50 CCTCATCACA GCAATATTTA ACAATTTATT CCTGATAAAA ATAATATTAA TTTATTTAAT 660  
 TAAAAAGAAT TCTTCCAAAA AAAAAAAAAA AAAAAAACNT CG 702

55

(2) INFORMATION FOR SEQ ID NO: 32:

60

(i) SEQUENCE CHARACTERISTICS:

180

(A) LENGTH: 1142 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

	CGGCACGAGG AAGAAATGGC AGAGACTGGA ATCTCTCTTC ATGAAAAAAT GCAGCCCCCTT	60
10	AACTTCAGTT CGACAGAGTG CAGCTCCTTC TCTCCACCCA CCACAGTGAT TCTCCTTATC	120
	CTGCTGTGCT TTGAGGGCCT GCTCTTCCTC ATTTTCACAT CAGTGATGTT TGGGACCCAG	180
15	GTGCACTCCA TCTGCACAGA TGAGACGGGA ATAGAACAAT TGAAAAAGGA AGAGAGAAGA	240
	TGGGCTAAAA AAACAAAATG GATGAACATG AAAGCCGTTT TTGGCCACCC CTCTCTCTA	300
	GGCTGGGCCA GCCCCTTTGC CACGCCAGAC CAAGGAAGG CAGACCCGTA CCAGTATGTG	360
20	GTCTGAAGGA CCCCGACCGG CATGGCCACT CAGACACAAG TCCACACCAC AGCACTACCG	420
	TCCCATCCGT TCTCATGAAT GTTTAAATCG AAAAAGCAAA ACAACTACTC TTAAACTTTT	480
25	TTTTATGTCT CAAGTAAAT GGCTGAGCAT TGCAGAGARA AAAAAAGTC CCCACATTTT	540
	ATTTTTTAAA AACCATCCTT TCGATTCTT TTGGTGACCG AAGCTGCTCT CTTTTCCTTT	600
	TAAAATCACT TCTCTGGCCT CTGGTTTCTC TCTGCTGTCT GTCTGGCATG ACTAATGTAG	660
30	AGGGCGCTGT CTCGCGCTGT GCCCATCTA CTAAGTGTGAGT GAGACATGAC GCTGTGCTGG	720
	GATGGAATAG TCTGGACACC TGGTGGGGGA TGCATGGGAA AGCCAGGAGG GCCCTGACCT	780
35	TCCCACTGCC CAGGAGGCAG TGGCGGGCTC CCCGATGGGA CATAAACCT CACCGAAGAT	840
	GGATGCTTAC CCCTTGAGGC CTGAGAAGGG CAGGATCAGA AGGGACCTTG GCACAGCGAC	900
	CTCATCCCCC AAGTGGACAC GGTTCGCTG CTAAGTGC AAGCAATTGC CTGCCTTGTA	960
40	CTTTATGGGC TTGGGGTG TGAGATGATT TTGCGGGGGA GTGGGGGAGA AAGATGAAAG	1020
	AGGTCTTATT TGTATTCTGA ATCAGCAATT ATATTCCCTG TGATTATTG GAAGAGTGTG	1080
45	TAGGAAAGAC GTTTTCCAG TTCAAAATGC CTTATACAAT CAAGAGGAAA AAAAAAAAAA	1140
	AG	1142

50

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:

55

(A) LENGTH: 928 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

60

GGCACGAGGT CTAATGAGGG CTCTCTTGTT TGCTAGAGAT GAGAGAAATG TATACTAATC 60  
 ATTTTAATTT GTACTTAAAA TACATTTTAC TAATCATATT GATTTTAAAT ATGACAAATT 120  
 5 CTCTAGTAG AACTAATCT TTCTTGTTTA TCATATTGTC CTAGAGAAGC CTAGGTAAAA 180  
 ATGGGTTCCTA CCTAGTCTGT TTGTATAACA CCTTCCCCCG TCCCCTCTCC ATCCCTGCCA 240  
 ATTGGGCTCT ATGCATATTG ACAAGCAAAT AAGAAAACCT TAGGTTCCTG TATTTGAATT 300  
 10 TCCAAAACAA TAAAAGGTTT TGAACAAGA TTTGCATTCA AGAAGAGGCA GAAATTTTGT 360  
 CTTATCTTTT TATCATTTTG TGAACCTGTG TTTCTCTGTA TGCTTAGAAA ATTTACACAC 420  
 15 AAGGAATGTT TGAAAAAGTG AGAATTTTAG AGTGCTGGG TGGTTTTTAT TTGGTCAGTG 480  
 CTGATGTGTT AGGTGTTTAG GGAAATAATG CTTGAGGACC TTTTGACAA CACAGCTTCA 540  
 TGAATGACTG GGGGATATTT ATGTTTGTGC TGAGAAAAGG GAGGGAGTGG GCAGGTGGGA 600  
 20 GTGGGGACCT TTCCATTGAA AGCAGTGCAG TCAGCTGTTT CGTAGATGCA TTTTCTTTT 660  
 ATGCTTGTA CATTGTTCTT GTGTCCATAA TTGACTGAAA TGTCAGCTC CAGGAATGCA 720  
 25 AGGCATTTAT CAGGTGACCA GAAGTAGAAC CTTGTTGATT ATGAAATGGA AGAATAATGT 780  
 CAAGGTAGTG GGGGTAAAAT GACAAATAAG ATTTTACTGG TGAATTTCCA TGCTTAGTAT 840  
 GTACATTAAC CTCTTTTAA GTTGCATGTT AATCTGGTAT AACGTATTGT GTCTGGTTTA 900  
 30 TGCTTTGAGT AAAAAAAAAA AAAAAAAA 928

35

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

40

- (A) LENGTH: 773 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

45

GGCACGAGTT CTGGCCTCTC ATTTCCCTAC ACTCTGACAT GAATGAATTA TTATTATTTT 60  
 TCTTTTCTT TTTTFTTTT ACATTTTGTA TAGAAACAAA TTCATTTAAA CAACTTATT 120  
 50 ATTATTATTT TTTACAAAAT ATATATATGG AGATGCTCCC TCCCCCTGTG AACCCCCAG 180  
 TGCCCCGTG GGGCTGAGTC TGTGGGCCCA TTCGGCCAAG CTGGATTCTG TGTACCTAGT 240  
 ACACAGGCAT GACTGGGATC CCGTGTACCG AGTACACGAC CCAGGTATGT ACCAAGTAGG 300  
 55 CACCCTTGGG CGCACCCTT GGGGCCAGG GTCGGGGGAT GTTGGGAGCC TCCTCCCCAC 360  
 CCCACCTCCC TCACTTCACT GCATTCCAGA TTGACATGT TCCATAGCCT TGCTGGGAA 420  
 60 GGGCCCACTG CCAACTCCCT CTGCCCCAGC CCCACCCTG GCCATCTCCC TTTGGGAAC 480

5 AGGGGGCTGC TGGTGGGAAA TGGGAGCCAG GGCAGATGTA TGCATTCCCTT TATGTCCCTG 540  
 TAAATGTGGG ACTACAAGAA GAGGAGCTGC CTGAGTGGTA CTTTCTCTTC CTGGTAATCC 600  
 TCTGGCCCGAG CCTTATGGCA GAATAGAGGT ATTTTATAGC TATTTTGTGA ATATGGCTTC 660  
 TGGTCAAAAT CCCTGTGTAG CTGAATCCC AAGCCCTGCA TTGTACAGCC CCCCACTCCC 720  
 10 CTCACCACCT AATAAAGGAA TAGTTAACAC TCAAAAAAAA AAAAAAAAAA AAA 773

15 (2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 453 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

25 TAAAAATGTTA CACGCTTGTC ATATTCCAGG CACTGCACTA TGTATGCCGT TTATCAACAG 60  
 TTAGCTCAGC TAACCCTCAT GGTAACCTTG TTAGCCCCGA TTTTGCCAGA TGAGCAAAGT 120  
 GAGGTTTTTG AGGCCCTAAG TAACTTGCCC AAGGTCACGT GGCTGGGAAG TAACTCTCCC 180  
 30 AGTTCTGAGA TGCCCCGAGCC TGGACGCTTT GTCATTGTAC ACCATCAACT CAGTGCTGCC 240  
 AGTCATTCCA GCAGCCAGCT ACGGTAGTCA AGGTTTCTCC ACCTTAGCAC TGTGACATT 300  
 35 TCGAGCCAGA TAATCTCTG TGGTGAGGAG CTGTCCTATG CCTTGTAGGA TATACAACAG 360  
 CATCTGCGCT TTACCCACCA GATGYTGGAA CACCTCCCCA GTCGTGACAG CCCAAAATGT 420  
 CTATAGACGT TGCCACGTAT ACCCAGGGGT TCC 453  
 40

45 (2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 459 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

55 GTGACTGCCG CCCTGCCCCG AGCCATGTGG CCCCCGCTGT TGCTGCTGCT GCTGCTGCTC 60  
 CCGGCCGCCC CGGTCCCCAC CGCCAAAGCC GCTCCCCACC CGGATGCTAA CACCCAGGAA 120  
 GGCCTTCAGA ACCTGCTCCA AGGAGTCGGG GCTGGCGGAG ACGGAGAGCT GCGGGCAGAC 180  
 60 TCACACCTGG CCCCAGGCTC TGGCTGTATT GATGGGGCTG TGGTGGCCAC GCGACCAGAA 240

AGCCGGGGAG GAAGACCTGC GGTTCCTGA GAGGCGTCCA GGGCTGCAGG CCACGGCGAC 300  
 5 AGGCTCCGGG GAACATGGGG CTTTCCCTGT CCACTCCCAA GGAGTGTGGG CCTCAACGCA 360  
 TTGGCAGGGG ACGGCCGTGT GCCCTCTYCA GACCCACCCC CCAGATGCAT TTATTAGAAA 420  
 TAATAAATTC TTTCTTAGCT AAAAAAAAAA AAAAAAAT 459

10

(2) INFORMATION FOR SEQ ID NO: 37:

15

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 509 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

ATGAAATTTA CCACTCTCCT CTTCTTGGCA GCTGTAGCAG GGGCCCTGGT CTATGCTGAA 60  
 25 GATGCCTCCT CTGACTCGAC GGGTGCTGAT CCTGCCCAGG AAGCTGGGAC CTCTAAGCCT 120  
 AATGAAGAGA TCTCAGGTCC AGCAGAACCA GCTTCACCCC CAGAGACAAC CACAACAGCC 180  
 CAGGAGACTT CGGCGGCAGC AGTTCAGGGG ACAGCCAAGG TCACCTCAAG CAGGCAGGAA 240  
 30 CTAAACCCCC TGAAATCCAT AGTGAGAGAA AGTATCTTAC TAACAGAACA AGCCCTTGCA 300  
 AAAGCAGGAA AAGGAATGCA CGGAGGCGTG CCAGGTGGAA AACAATTCAT CGAAAATGGA 360  
 35 AGTGAATTTG CACAAAAATT ACTGAAGAAA TTCAGTCTAT TAAACCATG GGCATGAGAA 420  
 GCTGAAAAGA ATGGGATCAT TGGACTTAAA GCCTTAAATA CCCTTGTAGC CCAGAGCTAT 480  
 TAAACGAAA GCATCCAAA AAAAAAAAAA 509  
 40

(2) INFORMATION FOR SEQ ID NO: 38:

45

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 598 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: linear

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

ATGTGGGCT GTGGGATCCC AGCGCTGGGC CTGCTCCTGC TGCTGCAGGG CTCGGCAGAC 60  
 55 GGAAATGGAA TCCAGGGATT CTTCTACCCA TGGAGCTGTG AGGGTGACAT ATGGGACCGG 120  
 GAGAGCTGTG GGGGCCAGGC GGCCATCGAT AGCCCAACC TCTGCCTGCG TCTCCGGTGC 180  
 60 TGCTACCGCA ATGGGGTCTG CTACCACCAG CGTCCAGACG AAAACGTGCG GAGGAAGCAC 240

ATGTGGCGGC TGGTCTGGAC GTGCAGCGGC CTCCTCCTCC TGAGCTGCAG CATCTGCTTG 300  
 TTCTGGTGGG CCAAGCGCCG GGACGTGCTG CATATGCCCG GTTTCCTGGC GGGTCCGTGT 360  
 5 GACATGTCCA AGTCCGTCTC GCTGCTCTCC AAGCACCGAG GGACCAAGAA GACGCCGTCC 420  
 ACGGGCAGCG TGCCAGTCGC CCTGTCCAAA GAGTCCAGGG ATGTGGAGGG AGGCACCGAG 480  
 10 GGGGAAGGGA CGGAGGAGGG TGAGGAGACA GAGGGCGAGG AAGAGGAGGA TTAGGGGAGT 540  
 CCCC GG GGA CTGGTCAATA CAGATACGGT GGACGGAAAA AAAAAAAAAA AAAAAAAA 598

15

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:  
 20 (A) LENGTH: 454 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

ATGGAGGCTG TTTTACAGT TTTT TTTT GTTGTGTTT TGTTT TAAA GAATACAGAA 60  
 GGAGCCAAGC TTTT TGCAC TTTGTATCCA GCTGCAAGCT CAGGGCAGAG TCAAGGGCCT 120  
 30 GGGTTGGAAA AACCTGACTC ACAGGAATGC ATAATGACC CTTGCAGCTA CCAATAGCC 180  
 CTGGAGCTG GCACTGAACC AGGCTGCAAG ATTTGACTGC CTTAAAAACA CAAGGCCCTC 240  
 35 TAGGCCTGGC AGGGATGTCC CTGTGCCCAG CACTGGGGGC TCGAAGACTG GTTCTAGCA 300  
 CTACCGTCA CGCCATGTC GTCCTAGAAG GGTCCAGAAG ATTATTTTAC GTTGAGTCCA 360  
 TTTT TAATGT TCTGATCACC TGACAGGGCA CCCC AAACCC CCAACTCCA ATAAAGCCG 420  
 40 TGACGTTCCG ACAAAAAAAA AAAAAAAA AAAA 454

45

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:  
 50 (A) LENGTH: 425 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

GCTAAAGGCC ATTCCCTCCG CAGGCATTT GCGTCGGGT GGGAGGGGAA AACGCATCTT 60  
 GTTAATTATT TTTAATCTA TTTATTGTAC ATACCTGGGG CAGGGGCTTG GGGAGGTGGA 120  
 60 GGGGGRAGAA GGGTCCCCTC TCTCTGCCCC TCCCCTCTT TTTCTACGGC GATTGTGCTG 180

TGTCTGGCCC CCACCCACTG MCCATCCCCC ATTGTTGTCT GGATGTGGTT CTATTTTTTA 240  
 TCGGTCTCCT TTCCCCTCCT CCCCGTFTYC GCGCCCGMCC CACCCCTGC TCCCACTACC 300  
 5 CTTTGTCTCT TGCTCTTTCT TGGGYTTCTG TACAAC TCA CTTGTATACA CTGTGTACAC 360  
 ACAACCAGYC WAACGCAAAA CCCAACGGCA AACACTTTAA AAAAAAAAAA AAAAACTGG 420  
 10 GGGGT 425

15 (2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2471 base pairs  
 (B) TYPE: nucleic acid  
 20 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

25 GGACAGAGTA TGGCTTCCCG TGGACTCAGC CTCTTCCCG ANTCTGGCA CGAGGGGGCT 60  
 TCGCGTCTGT GCTTCTGTG GCTGACGTA TCTGGAGGAG ATTGCTTTC TTTTCTCCA 120  
 AAAGGGGAGG AAATTGAAAC TGAGTGGCCC ACATGGGAA GAGGGGAAAG CCCAGGGGTA 180  
 30 CAGGAGGCCT CTGGGTGAAG GCAGAGGCTA ACATGGGGT CGGAGCGACC TTGGCCGTTG 240  
 GCCTGACCAT CTTTGTGCTG TCTGTGTA CTATCATCAT CTGCTTCACC TGCTCTGCT 300  
 35 GCTGCCTTTA CAAGACGTGC CGCCGACCAC GTCCGGTTGT CACCACCACC ACATCCACCA 360  
 CTGTGGTGCA TGCCCTTAT CCTCAGCCTC CAAGTGTGCC GCCCAGCTAC CCTGGACCAA 420  
 GCTACCAGGG CTACCACACC ATGCCGCCTC AGCCAGGGAT GCCAGCAGCA CCCTACCCAA 480  
 40 TGCAGTACCC ACCACCTTAC CCAGCCGAGC CCATGGGCCC ACCGGCCTAC CACGAGACCC 540  
 TGGCTGGAGA GCAGCCGCGC CCTACCCGCG CAGCCAGCCT CTTACAACC CGGCCTACAT 600  
 45 GGATGCCCCG AAGGCGGCCC TCTGAGCATT CCCTGGCCTC TCTGGCTGCC ACTTGGTTAT 660  
 GTTGTGTGTG TCGGTGAGTG GTGTGCAGGC GCGGTTCTTT ACGCCCCATG TGTGCTGTGT 720  
 GTGTCCAGGC ACGGTTCTTT ACGCCCCATG TGTGCTGTGT GTGTCTGCC TGTATATGTG 780  
 50 GCTTCTCTG ATGCTGACAA GGTGGGAAC AATCCTTGCC AGAGTGGGCT GGGACCAGAC 840  
 TTTGTCTCTT TCCTCACCTG AAATTATGCT TCCTAAATC TCACCCAAA CTCAAAGAAT 900  
 55 GGGGTGGTGG GGGGCACCTT GTGAGGTGGC CCCTGAGAGG TGGGGGCTC TCCAGGGCAC 960  
 ATCTGGAGTT CTTCTCCAGC TTACCCTAGG GTGACCAAGT AGGGCCTGTC ACACCAGGGT 1020  
 60 GCGCAGCTT TCTGTGTGAT GCAGATGTGT CCTGGTTTCG GCAGCGTACC AGCTGCTGCT 1080

TGAGGCCATG GCTCCGTCCC CGGAGTTGGG GGTACCCGTT GCAGAGCCAG GGACATGATG 1140  
 CAGGCGAAGT TGGGGATCTG GCCAAGTTGG ACTTTGATCC TTTGGGCAGA TGTCCCATTG 1200  
 5 CTCCCTGGAG CCTGTCATGC CTGTTGGGGA TCAGGCAGCC TCCTGATGCC AGAACACCTC 1260  
 AGGCAGAGCC CTA CTCTCAGCT GTACCTGTCT GCCTGGACTG TCCCCTGTCC CCGCATCTCC 1320  
 10 CCTGGGACCA GCTGGAGGGC CACATGCACA CACAGCCTAG CTGCCCCCAG GGAGCTCTGC 1380  
 TGCCCTTGCT GGGCCTGCCC TTCCCACAGG TGAGCAGGGC TCCTGTCCAC CAGCACACTC 1440  
 AGTTCTCTTC CCTGCAGTGT TTTTCATTTA TTTTAGCCAA ACATTTTGCC TGTTTTCTGT 1500  
 15 TTCAAACATG ATAGTTGATA TGAGACTGAA ACCCCTGGGT TGTGGAGGGA AATTGGCTCA 1560  
 GAGATGGACA ACCTGGCAAC TGTGAGTCCC TGCTTCCCGA CACCAGCCTC ATGGAATATG 1620  
 CAACAACCTCC TGTACCCAG TCCACGGTGT TCTGGCAGCA GGGACACCTG GGCCAATGGG 1680  
 20 CCATCTGGAC CAAAGGTGGG GTGTGGGGCC CTGGATGGCA GCTCTGGCCC AGACATGAAT 1740  
 ACCTCGTGT CCTCCTCCCT CTATTACTGT TTCACCAGAG CTGTCTTAGC TCAAATCTGT 1800  
 25 TGTGTTTCTG AGTCTAGGT CTGTACACTT GTTTATAATA AATGCAATCG TTTGGAAAAA 1860  
 AAAAAAAAAA AAACCTCGTAG GGGGGGCCCC TACCCAATGG GCYCMARAT AGTAGARWAC 1920  
 RAAAYAMCA ANTGCAACCA AAGAGGGGCC AGGGGANPTT TAAGAGGGCC CCTTTTGGG 1980  
 30 GGNATCCANT TTAGCCGGGG TTNNTAAGGG AAGTTGCNTG GCGGGGGTTA GGGCCCSGTT 2040  
 KYTWCTTCCA ACCAAGGGTT YTYGTGGTTA GGCCGGGTTG GGCCCMATGG GCTGGGCTGG 2100  
 35 GTAAAGTGGT GGGTMAYTGC MATTTGGGTAG GGTGCTGCTG GCATTCTCTG CTGAGGCGGC 2160  
 ATGGTGTGGT AGCCCTGGTA GCTTGGTCCA GGGTAGCTGG GCGGCACACT TGGAGGCTGA 2220  
 GGATAAGGGG CATGCACCCA CAGTGGTGA TGTGGTGGTG GTGACAACCG GACGTGGTCG 2280  
 40 GCGGCACGTC TTGTAAAGGC AGCAGCAGGA GCAGGTGAAG CAGATGATGA TAGTGACGAC 2340  
 AGACAGCACA AAGATGGTCC AGCCAACGGC CAAGGTCGCT CCGAACCCCA TGTTAGCCTC 2400  
 45 TGCCTTCACC CAGAGGCCTC CTGTACCCCT GGGCTTTCCC CTCTTCCCAT CGTGGGCCAC 2460  
 TCACTCGTGC C 2471

50

(2) INFORMATION FOR SEQ ID NO: 42:

- 55 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 2659 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:



	GGCACGAGCT TTTCTCTAGA GTCTGAAAGA TGCTAGAAAG AAATAAAATT TAACTTACTTT	60
5	AAGAGAATTA TGGATCTTTT ATTAATAAAA ATTAAC TTGA TGATTGTAAC TAACAGTTAT	120
	GATAATTC TG GTATTTATAG CTMTTTTAT TCCCCTGCAG AAAACCATAG GCAAAATTGC	180
	AACATGCTTG GAATTGCGAA GTGCAGCTTT ACAGTCCACA CAGTCTCAAG AAGAATTTAA	240
10	ACTGGAGGAC CTGAAGAAGC TAGAACCAAT CCTAAAGAAT ATTCTTACAT ATAATAAAGA	300
	ATTCCCATTT GATGTT CAGC CTGTCCCATT AAGAAGAATT TTGGCACCTG GTGAAGAAGA	360
15	GAATTTGGAA TTTGAAGAAG ATGAAGAAGA GGGTGGTGCT GGAGCAGGTC TCCTGATTCT	420
	TTCTGCTAG AGTTCCCGGT ACTTTATTAC CAAGGTGGCC ATCGGAACCA GGAATGACAT	480
	TACTCACTAT CAGAATTGAG AAAATTGGTT TGAAAGATGC TGGGCAGTGC ATCGATCCCT	540
20	ATATTACAGT TAGTGTAAG GATCTGAATG GCATAGACTT AACTCCTGTG CAAGATACTC	600
	CTGTGGCTTC AAGAAAAGAA GATACATATG TTCATTTTAA TGTGGACATT GAGCTCCAGA	660
25	AGCATGTTGA AAAATTAACC AAAGGTGCAG CTATCTTCTT TGAATTCAAA CACTACAAGC	720
	CTAAAAAAG GTTTACCAGC ACCAAGTGTT TTGCTTTCAT GGAGATGGAT GAAATTAAAC	780
	CTGGGCCAAT TGTAATAGAA CTATACAAGA AACCCACTGA CTTTAAAAGA AAGAAATTGC	840
30	AATTATTGAC CAAGAAACCA CTTTATCTTC ATCTACATCA AACTTTGCAC AAGGAATGAT	900
	CCTGACATGA TGAACCTGGA ACTTCTGTGA ATTTTACCAC TCAGTAGAAA CCATCATAGC	960
35	TCTGTGTAGC ATATTACCCC TTCAACAGGC AGGAAGCAAG CCGTACCCAG ACCAGTAGGC	1020
	CGGACGGAGT CAAATGCAAA GCTGTACCAC AGAATTCAGA GTCCAGCACA TCACACTGAC	1080
	GTATAGGACT CCTTGGGATA CAGGTTTATT GTAGATTTTG AAACATGTTT TTACTTTTCT	1140
40	ATTAATGTG CAATTAATAG TCTATTTTCT AATTTACCAC TACTCCTACC CTGCTTCTG	1200
	GAACAATACT GTTGTTGGTA GGATGTGCTC ATCTTCAGAC TTAATACAGC AATAAGAATG	1260
45	TGCTAGAGTT TACACATCTG TTCACTTTTG CTCCAATATG CTCTTTTGAC TTAACGTCAA	1320
	GCTTTGGGTT GATGTGGTA GGGTAGTGT CAACTGCTTT GAGAGGAATG GGACCAGTTC	1380
	TGCTGCCTAA GAAGGTCTGT CTGGATGTTT ATAGGCAGCA CCTCTGAAGT GGCCTAAATT	1440
50	CACCCTGATC TGATAGTTTT CTGCTTAGA AAGTGTGCCT TGGCCAGATC AGTATCCCAC	1500
	ATGGGAGTGT TCCCTAGGTT GTAGCTGTGA TTGTTTCCAG ATGACCAGAT TGTMTTCTG	1560
55	AAAATGAGCA TATTTT TAGT CATGTCGATT AGCTGTTCTT CTACATCACA TTGTTACTCT	1620
	TTCTGATGAT GATTCTAGGG TTAACATTGG AACCATCTCA AAATAATTAC AAAGTTTTAG	1680
	ATGGGTTTAC AATGCTTCT AAACAATGTA ATCTAAAAAT AATTGAGTCA GATGCTAACG	1740
60	AGATACTGCA GGCATAACTG CTGTTTTTCT GACAAC TGATGAAACCT TAAACCTGC	1800

5 ATACCTCTTC TTACAGTGAG GAGTATGCAA AATCTGGAAA GATATTCTAT TTTTITTTATA 1860  
 TAGGTAGATA GGATCGCCAT TTATTTCCTA TTTAGATATA CTGACATTCA TCCATATGAA 1920  
 AATATGCAGG TCATTAGCTT ACTATAATTT ACTTTTGACT TAATGGGGCA TAAATAAAAC 1980  
 TTTCATAGTA CACATGAGGT GGATATTMGA TACACAGAAC ATTTGCGGTG GGCTTTCTGT 2040  
 10 GGGTTAGATG TAAAGCCAC ATATTTTAAT ATTCACTATT TTAAATGAGC AATGCATGAG 2100  
 GGGAAATGCAG TGTCAGTACC TGGCCTATTT TTAAACTAGT GTAATCACCC TAGTCATACC 2160  
 ATTCAGTATG TTTGCTTTTT AAAATAAGTA ACCACAATTA AGTTGTTGTA GCCCTTGCAC 2220  
 15 TTCAAGAGAT CTAGTCTTTA CTTTCAGTTG TCTGTTAGGT CCATTCTGTT TACTAGACGG 2280  
 ATGTTAATAA AACTATGCG AGCCTGGAAT GGAATTCTCC AGCCAAATTT TAGTCTTGTC 2340  
 20 CTCTCCATCT TGATTGGATT AATTCCAAAT TCTAAATGA TTCAGTCCAC AATAGCTCTA 2400  
 GGGGATGAAG AATTTGCCCTT ACTTTGCCCA GTTCCTAAGA CTGTGAGTTG TCAAATCCCT 2460  
 AGACTGTAAG CTCCTCAAGG AGCAAGAGGC GCATTTTCTC CGTGTGATGT AATTTTCTA 2520  
 25 AGGTGTTTGG CAGCACTCTG TACCCTGTGG AGTACTCAGT ACCTTTTGTT TGATGTTGCT 2580  
 GACAAGACCT GAAAAAAAT CCCTTAAAAA AAAAACCCAT TAAAGTGTAG CAAAACCGAA 2640  
 30 AAAAAAAAAA AAAAAAAAAA 2659

35 (2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 1635 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

45 CGAGGAGGTC ATGAACAAGG AGGCGGGAGA GGTGGACGTG GTGGCTATGA CCATGGTGGC 60  
 CGAGGGGGAG GAAGAGGAAA TAAGCATCAA GGAGGCTGGA CAGATGGAGG GAGTGGTGGG 120  
 GGAGGTGGCT ACCAAGATGG TGGTTATCGA GATTCAGGTT TCCAGCCAGG TGGCTATCAT 180  
 50 GGTGGCCACA GCAGTGGTGG CTATCAAGGC GGAGGTTATG GTGGCTTCCA AACATCTTCT 240  
 TCMATACAG GAAGTGGATA CCAGGTGGT GGCTACCAGC AGGACAATAG ATACCAAGAT 300  
 55 GGCGGCACC ATGGTGATCG TGGTGGTGGT CGTGGTGGGC GAGGTGGTGG TGCAGGCCGA 360  
 GGTGGTCGTG CAGGCCAGG AGGAGGCTGG GGAGGAAGAG GGAGCCAGAA TTATCACCAA 420  
 60 GGGGGTCAAT TTGAACAGCA TTTCCAGCAT GGAGGTTATC AGTATAATCA TTCGGATTT 480

	GGACAGGGAA GACATTACAC TAGTTGAGGC TACCGAACCT TACATTTTGC TAGAGCTCA	540
	GTAATAGAAA CTTAGTTTCA GAATCCTGAA TTCAGCACCT ATTTTGAATT AATGTGAGAC	600
5	CACAGGTGGC AGGCAGATTC CTGCTTGGCA TAAGCAATTG TAGGTCTTCA TTCAATTCTG	660
	TTAGATTTTT TTATTGGACT TACATAATGC CGTTTATTTG AGAAACACAT AACATCTCTC	720
10	CTTCTATGA AAAATTTTTT AAAAGGTGGT TAAAAATGCC TTTAATTGCC CAGTAGACTA	780
	ATTCCACAGT CAGAACATGC AAACTTTTT GAAGAAATTA CTTGAATAAG TAGTTTTCAT	840
	GTTTTCAATA TGCAGTTTTG AAAATGAGGA TTCACCTAGA CTTTTTTAGA TTTACTACYA	900
15	GGAAACCTTC CYCATATGAA TAACCATTTA TATGTGTTTT GCTTAAAGTA TTCCAATGCC	960
	TATTTTCCAA GCACAGTTCT GCGGGCGGT TGAATTTTAT GCCACGTGTG CTTTATGATG	1020
20	GAATTTTAG GTCAGTTCCT ATTAAATGAG CTCTTGTGCA GATAGCACAT TCAGTAGCCT	1080
	TATTTGTGTTG ATGGAATACT GTATCATATG CTCAACTCTG AAAACCTTGA ACACGGCCAA	1140
	AATCCATAAA GATTATAAAA GCAAACTAAG TTGTGAAGCT ATAGTACATG TAGGCATTTA	1200
25	GTTAAGTATA GCAATTCAAA CTGACCTGCA TCCATCCAAA ACAAATTCCT CCTTCAACCT	1260
	TATTTTACT TGAAATTTGC TAGAAGAAAT AGCAAACCGA AATTTGTTTT ATGCATGAGT	1320
30	TAATACCACT GGCTCAGCAA ATACAAGTTA GTTTGCTTTA AGCAGGTAAC TTTTTTGTGTA	1380
	ATGGAAGAAA TGCATACAA AGTTAAGACA GATTTTGTCT AAGTGCAGGA GGCCCTTTAT	1440
	TATTGCTGCA GAAACAAAA GCCTGGCTGA GTTGATGTTT TACATTCTCC CTTACTGAAA	1500
35	TCTACATGAC ATGATGCTTC TTGCTGGGTT TTTGTACATG TAAACATTGT CAAGCTGTGA	1560
	AAGAAAATGG CTGGAGGTGT GCTTTGTGTG AAAGGTGAGC ACTGAAAGTA TCTGTAAAGT	1620
40	TCTCCNGAAA AAAAA	1635

45 (2) INFORMATION FOR SEQ ID NO: 44:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 780 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: linear

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

55	AACATGGTCA TGTCTTTTAG TTTCATTATT TTCCTACTCC TTGTATGTCA AGAAATTACA	60
	TTTTGCATGT CTTATGGAGA TGCTGTTAAT TGCTTCAGTG AGTGCTTTTC TAATCTGCAG	120
	ACCATTTACA TTTCCTGTTT GCAGCATGCT GTGTGCAAAC AYTCAAGTAAT TTGGAGTATT	180
60	CAATTATTTG TTAGGGCTCT TCCTATTTCC AAATGTGCTG AATTGTCTAT TGATGGGATT	240

5 TTCAGATCTT TTCATGAGAA CTGGAAATGT AGCTGGGTGG CACCTACCTA GGTGCTACG 300  
 TAGTGAGTAG ACTTCTCTT GGGTATAGTA AGCCTCAGAC AGCTTTCCT TTTATCTACT 360  
 TTACTTGTGG AAATAAAACA GTCATTTTGT TCTGAAAGAA TAAGATAGCT TTCTGTAGAG 420  
 AAGGAATTCC TACCTCTAAA AGCTGCCTTG AGAACTCAGA ACTGGCAGTT TTCTGAGGTG 480  
 10 ATTTTAAAT TTCAGTATTA GGGAGAGTCC AGCATTTGCT GACACAGATT CTACATAACT 540  
 AATGTATGAT AGCAAATGCA AAACATTTAT AATGTGGTGT ATCTTGCGCA TACACAGGTT 600  
 AGAACAAGTA GACTCTGGCA GCAGATCTCC AGAGACCCAA GTTAGGTTT TCATAGTGTA 660  
 15 TTTGAAGTAG TTATACTCCT GGCTTAAGTA GTTTAGTGCC TGGGAGAATC CATTTACTGAA 720  
 AAGCATTTAA CTTAAAAAAA AAAAAAAAAA AAAACTGAAA AGGTAGTGAA TACAGAATAG 780  
 20

## (2) INFORMATION FOR SEQ ID NO: 45:

25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 2378 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

GCGAAGCAGC TGAAGCCGCC GCCGCGCAGA ATCCACGCTG GCTCCGTGCG CCATGGTCAC 60  
 35 CCACAGCAAG TTTCCCGCCG CCGGGATGAG CCGCCCCCTG GACACCAGCC TGGCCTCAA 120  
 GACCTTCAGC TCCAAGAGCG AGTACCAGCT GGTGGTGAAC GCAGTGCAGCA AGTGCAGGAG 180  
 40 AGCGGCTTCT ACTGGAGCGC AGTGACCGC GCGGAGGCGA ACCTGCTGCT CAGTGCCGAG 240  
 CCCGCCGCGA CCTTTCTGAT CCGCGACAGC TCGGGACCAG CGCCACTTCT TCACGCTCAG 300  
 CGTCAAGACC CAGTCTGGGA CCAAGAACTT GCGCATCCAG TGTGAGGGGG GCAGCTTCTC 360  
 45 TCTGCAGAGC GATCCCGGGA GCACGCAGCC CGTGSCCGC TTCGACTGCG TGCTCAAGCT 420  
 GGTGCACCAT TACATGCCG CCCCTGGAGC CCCCTCCTTC CCCTCGCCAC CTACTGAACC 480  
 50 CTCCTCCGAG GTGCCCCGAG AGCCGTCTGC CCAGCCACTC CCTGGGAGTC CCCCCAGAAG 540  
 AGCCTATTAC ATCTACTCCG GGGGCGAGAA GATCCCCCTG GTGTTGAGCC GGCCCTCTC 600  
 CTCCAACGTG GCCACTCTTC AGCATCTCTG TCGGAAGACC GTCAACGGCC ACCTGGACTC 660  
 55 CTATGAGAAA GTCACCCAGC TGCCGGGGCC CATTCGGGAG TTCCTGGACC AGTACGATGC 720  
 CCCGCTTTAA GGGGTAAAGG GCGCAAAGGG CATGGGTCGG GAGAGGGGAC GCAGGCCCTT 780  
 60 CTCCTCCGTG GCACATGGCA CAAGCACAAG AAGCCAACCA GGAGAGAGTC CTGTAGCTCT 840

	GGGGGGAAAG	AGGGCGGACA	GGCCCCCTCC	TCTGCCCCCT	CCCTGCAGAA	TGTGGCAGGC	900
	GGACCTGGAA	TGTGTGGAG	GGAAGGGGGA	GTACCACCTG	AGTCTCCAGC	TTCTCCGGAG	960
5	GASCCAGCTG	TCCTGGTGGG	ACGATAGCAA	CCACAAGTGG	ATTCTCCTTC	AATTCCTCAG	1020
	CTTCCCCCTCT	GCCTCCAAAC	AGGGGACACT	TCGGGAATGC	TGAACATAATG	AGAACTGCCA	1080
	GGGAATCTTC	AAACTTTCCA	ACGGAACTTG	TTTGCTCTTT	GATTTGGTTT	AAACCTGAGC	1140
10	TGTTTGTGGA	GCCTGGGAAA	GGTGAAGAG	AGAGAGGTCC	TGAGGGCCCC	AGGGCTGCGG	1200
	GCTGGCGAAG	GAAATGGTCA	CACCCCCCGC	CCACCCACAG	CGAGGATCCT	GGTGACATGC	1260
15	TCCTCTCCCT	GGCTCCGGGG	AGAAGGGCTT	GGGGTGACCT	GAAAGGGAAC	CATCCTGGTG	1320
	CCCCACATCC	TCTCTCCGG	GACAGTCACC	GAAAACACAG	GTTCCAAAGT	CTACCTGGTG	1380
	CCTGAGAGCC	CAGGGCCCTT	CCTCCGTTTT	AAGGGGAAG	CAACATTTGG	CACGAGATGG	1440
20	GCTGGTCAGC	TGGTCTCCTT	TTCTTACTCA	TACTATACCT	TCCTGTACCT	GGGTGGATGG	1500
	AGCGGGAGGA	TGGAGAGACG	GGACATCTTT	CACCTCAGGC	TCCTGGTAGA	GAATACAGGG	1560
25	GATTCTACTC	TGTGCCTCCT	GACTATGTCT	GGCTAAGAGA	TTGCGCTTAA	ATGCTCCCTG	1620
	TCCCATGGAG	AGGGACCCAG	CATAGGAAAG	CCACATACTC	AGCCTGGATG	GGTGGAGAGG	1680
	CTGAGGGACT	CACTGGAGGG	CACCAAGCCA	GCCCACAGCC	AGGGAAGTGG	GGAGGGGGGC	1740
30	GGAAACCCAT	GCCTCCCAGC	TGAGCACTGG	GAATGTCAGC	CCAGTAAGTA	TTGGCCAGTC	1800
	AGGCGCCTCG	TGGTCAGAGC	AGAGCCACCA	GGTCCCCTG	CECCGAGCCC	TGCACAGCCC	1860
35	TCCCTCTCGC	CTGGGTGGGG	GAGGCTGGAG	GTCATTGGAG	AGGCTGGACT	GCTGCCACCC	1920
	CGGGTGCTCC	CGCTCTGCCA	TAGCACTGAT	CAGTGACAAT	TTACAGGAAT	GTAGCAGCGA	1980
	TGGAATTACC	TGGAACAGTT	TTTTGTMTTT	GTTTTGTGTT	TTGTTTTTGT	GGGGGGGGGC	2040
40	AACTAAACAA	ACACAAAGTA	TTCTGTGTCA	GGTATTGGGC	TGGACAGGGC	AGTTGTGTGT	2100
	TGGGGTGGTT	TTTTTCTCTA	TTTTTTTGTG	TGTTTCTTGT	TTTTTAATAA	TGTTTACAAT	2160
45	CTGCCTCAAT	CACTCTGTCT	TTTATAAAGA	TTCCACTCCA	GTCCCTCTCT	CTCCCCCCTA	2220
	CTCAGGCCCT	TGAGGCTATT	AGGAGATGCT	TGAAGAACTC	AACAAAATCC	CAATCCAAGT	2280
	CAAACCTTGC	ACATATTTAT	ATTTATATTC	AGAAAAGAAA	CATTTTCAGTA	ATTTTATAATA	2340
50	AAGAGCACTA	TTTTTTAATG	AAAAAAAAAA	AAAAAAAAAA			2378

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1772 base pairs

(B) TYPE: nucleic acid

60

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

5	TCGACCCACG CGTCCGGGAG GATCCCCAGC CGGGTCCCAA GCCTGTGCCT GAGCCTGAGC	60
	CTGAGCCTGA GCCGAGCCGG GAGCCGGTCG CGGGGGCTCC GGGCTGTGGG ACCGCTGGGC	120
10	CCCCAGCGAT GCGGACCTTG TGGGAGGCC TTCTTCGGCT TGGCTCCTTG CTCAGCCTGT	180
	CGTGCCCTGGC GCTTTCGGTG CTGCTGCTGG CGCACTGTCA GACGCCGCCA AGAATTTCGA	240
	GGATGTCAAG TGTAAGTGTG TCTGCCCTCC CTATAAAGAA AAATTCCTGGG CATATTTATA	300
15	ATAAGAACAT ATCTCAGAAA GATGTGTGAT GCCTTCATGT TGTGGAGCCC ATGCCTGTGC	360
	GGGGGCCTGA TGTAGAAGCA TACTGTCTAC GCTGTGAATG CAAATATGAA GAAAGAAGCT	420
20	CTGTCACAAT CAAGGTTACC ATTATAATTT ATCTCTCCAT TTTGGGCCTT CTACTTCTGT	480
	ACATGGTATA TCTTACTCTG GTTGAGCCCA TACTGAAGAG GCGCCTCTTT GGACATGCAC	540
	AGTTGATACA GAGTGATGAT GATATTGGGG ATCACCAGCC TTTTGCAAAT GCACACGATG	600
25	TGCTAGCCCG CTCCCGCAGT CGAGCCAACG TGCTGAACAA GGTAGAATAT GGCACAGCAG	660
	CGCTGGAAGC TTCAAGTCCA AGAGCAGCGA AAAGTCTGTC TTTGACCGGC ATGTTGTCCT	720
30	CAGCTAATTG GGAATTGAA TTCAAGGTGA CTAGAAAGAA ACAGGCAGAC AACTGGAAAG	780
	GAAGTACTG GGTTTTGCTG GGTTCATTT TAATACCTTG TTGATTTTAC CAACTGTTGC	840
	TGAAGATTTC AAAACTGGAA GKAAAACTT GCTTGATTTT TTTTCTTGT TAACGTAATA	900
35	ATAGAGACAT TTATAAAGC ACACAGCTCA AAGTCAGCCA ATAAGTCTTT TCCTATTGT	960
	GACTTTTACT AATAAAAATA AATCTGCCTG TAAAATAAAT TAAAAAATCC TTTACCTGGA	1020
40	ACAAGCACTC TCTTTTTCAC CACATAGTTT TAAGTTGACT TTCCAAGATA ATTTTCAGGG	1080
	TTTGTGTGT TGTGTGTGT TGTGTGTGT TTTGGTGGG AGAGGGGAGG GATGCCTGGG	1140
	AAGTGGTTAA CAACTTTTTC CAAGTCATTT TACTAAACAA ACTTTTGTA ATAGACCTTA	1200
45	CCTTCTATTT TCGAGTTTCA TTTATATTTT GCAGTGTAGC CAGCCTCATC AAAGAGCTGA	1260
	CTTACTCATT TGACTTTTGC ACTGACTGTA TTATCTGGGT ATCTGCTGTG TCTGCACTTC	1320
50	ATGGTAAACG GGATCTAAAA TGCCTGGTGG CTFTTCACAA AAAGCAGATT TTCTTCATGT	1380
	ACTGTGATGT CTGATGCAAT GCATCTAGA ACAAACTGGC CATTTGCTAG TTTACTCTAA	1440
	AGACTAAACA TAGTCTTGGT GTGTGTGGTC TTACTCATCT TCTAGTACCT TTAAGGACAA	1500
55	ATCCTAAGGA CTGGGACACT TGCAATAAAG AAATTTTATT TTAAACCCAA GCCTCCCTGG	1560
	ATTGATAATA TATACACATT TGTGAGCATT TCCGGTCGTG GTGAGAGGCA GCTGTTTGAG	1620
60	CTCCAATGTG TGCAGCTTTG AACTAGGGCT GGGGTGTGG GTGCCTCTTC TGAAAGGTCT	1680

5      AACCATTATT GGATAACTGG CTTTTTTTCT TCCTCTTTGG AATGTAACAA TAAAAATAAT      1740  
       TTTTGAAACA TCAAAAAAAA AAAAAAAA AA      1772

10      (2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:  
       (A) LENGTH: 1107 base pairs  
       (B) TYPE: nucleic acid  
       (C) STRANDEDNESS: double  
 15      (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:  
 20      CCGGCGAGAA GGGCAGACGG GACATGCAGC CTCTTCCGCC TGAGCCCCGG AAGTGATGTG      60  
       GCTGCGGCAT CGCGGCCTCG CTATGTCTGC CATTTTCAAT TTTCAGAGTC TATTGACTGT      120  
       AATCTTGCTG CTTATATGTA CCTGTGCTTA TATTCGATCC TTGGCACCCA GCCTCCTGGA      180  
 25      CAGAAATAAA ACTGGATTGT TGGGTATATT TTGGAAGTGT GCCAGAATTG GTGAACGGAA      240  
       GAGTCCTTAT GTTGCAGTAT GCTGTATAGT AATGGCCTTC AGCATCCTCT TCATACAGTA      300  
       GCTGGGGAAA ATGCCAGAAT GTAGTTGCCA TCAGATTGTA TTGTGAACAA GGACTGACTG      360  
 30      CAGAAAATAA TGGAAAGGAT GTTTAACTCT TTTATCTCCG AACATTGAAT GAGATAAATT      420  
       TCCAGATGCT GTTCTCTATT TTAATGTTAT TGGACCAATG TTCTGTATAA ACAATTAAGA      480  
 35      TGTAACCATT TAATAGTCTG TAACAATCAA CCTCAGTACT GTCACTACAA TATTACATTC      540  
       TGCAAAATGTT ATTCTGTTGT ATCAGATACA AAATTTTAGT GAGGTATCTC TAAGGCACAT      600  
       AGTAGAAAAC AAAATTGGTT AATTACTCAA GTTCCTTTCA CTGTGATTG GAAATGATTT      660  
 40      AATCTTTATA GAATGAGAAC CTTTTTTGGA CTAGCTTTTT TATTAAAATG GCTCAATTG      720  
       TGTGATAAG GATTGCATTA ATATTTAATA GTGCTTGCTT TTCCTCTGGG CACACCATT      780  
 45      TGATCATTA CCAGAGTACC TCTACTCTTA GCAAACCTA GTTTATGACA AGTATTTAAA      840  
       ATATTTAAAA CAAGCTTATG CAGTTCTTAA GGACGAAGGT AAATGAGATG TAACTTAAAA      900  
       ATAGTATTGG GAAAATGTTG ATAGTTAACA TTAGTGATT TAGACTAGCC AAATGACATA      960  
 50      GTAGGCTCTG AACATCTTG TCAAGTATAT GTATTTGTG CATGAATTTT TGCTGGAAAG      1020  
       CTGTCTTTCT CTGAAAAACA CAACGTTCTT AGAATGAAAA GAACAATTAT AAAATAAAAA      1080  
 55      AAAAATTTAA AAAAAACTGG GCGGGG      1107

60      (2) INFORMATION FOR SEQ ID NO: 48:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 805 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

10 TGCAGAAGAG ATGGAGTTGC TGTTGGAAAA CTACTACCGA TTGGCTGACG ATCTCTCCAA 60  
TGCAGCTCGT GAGCTTAGGG TGCTGATTGA TGATTCACAA AGTATTATTT TCATTAATCT 120  
GGACAGCCAC CGAAACGTGA TGATGAGGTT GAATCTACAG CTGACCATGG GAACCTTCTC 180  
15 TCTTTCGCTC TTTGGACTAA TGGGAGTTGC TTTTGGAAAT AATTGGAAT CTTCCCTTGA 240  
AGAGGACCAT AGAATTTTTT GGCTGATTAC AGGAATTATG TTCATGGGAA GTGGCCTCAT 300  
20 CTGGAGGCGC CTGCTTTCAT TCCTTGGACG ACAGCTAGAA GCTCCATTGC CTCCTATGGT 360  
ATGAAGGATA TGGTTCACGG CGGTATTGTG GAAGGGTTAT GATCATGGGC CCTAAAGTCA 420  
GAGCGCCTGG GATTAAGTTG TCACAGGCAC TATGGCCCTT GCGAGTTGCT TTCTCAAAC 480  
25 TCCTTCAGTT TCCCTATCTG TCAGTTAAGT CGGTATTACC TGCTTCATAG GGTATGGGA 540  
AGAATTAAAC AATATGTGTA AAGCACTTAC TAGCACACTG CCTAACACAA TAAGTTAGAA 600  
30 ATATAATTTG TGTAGAACTC TGACAACATA CATTTAAACA GATGTTAGTA ATTCTGGTAT 660  
AAGGTTTGTC ATAACCAAAT GGAAATGTAG GAAACATTTA TAATGTTCTT AAAAGATAGR 720  
AAATTCACCT CCATTTTCTT TGTACTTGAA GATGGCACCA CTGGAATAAA TACTTAAGAC 780  
35 ACTGAAAAAA AAAAAAAAAA AACTC 805

40

## (2) INFORMATION FOR SEQ ID NO: 49:

## (i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 1408 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

50 TCATTATTTA TTCATGTGGC TGAAAGAGTA TATTAATTAT GTTTAGATTT TTGGAAAAAG 60  
TCTGAACAAA AAAAGGACCT ATACAGTGCT CAACTATAT TTTTAAATTT ACTATTTTAT 120  
55 TTTTACTCAC ATATGAAAAA AATGGCTGTA CTATCATGTT TACATACATA CTAACATTGG 180  
AAACAGAATA ACGAATTGTA TTTAAATTTT ATGAAGAACA CACAAACATT AAAACACTGA 240  
TTGGTTACAG AAAGCAGAGT TTGAGGAAAA AACATTAGCT ATAATTTTCA TTTTCATTAA 300  
60



	AGAGCAGCAC CCTCTGAGAA TAATCAAACCT GATTAGTAAT ATTCATCTAT ACTGCAAAAT	360
	AATATGTACA AAGGAAAGTT AGTGATTGTA CTGATTTTAT TACTTTTACC AAGCCATTTT	420
5	ATGTTCCCTCA CTCAATGCAA AGAAATAAAA CATAATCTGA AGAAAAATAT GTCCTTATTA	480
	TTATTACAA TAAAAAGTTG GCTTTATTCT GCAAGCCTGG GCATATTGTA CAATTGGCAG	540
10	CACTTAACGG CTCAAGTGA TCAATGTACC AGTTTGATTC TGATCCACTG AATAGAATCT	600
	CTCATCCATA TCTGGTGACC AGACTAATC CATGGGAGCT GTGATAGACT GAACCATTTT	660
	TGTGGTATCC CTAGATCTCA CTAAATAAGA AAGACCCTAC ACCAGAAAAT ATAGCAACTG	720
15	ATCTATCTAT AAATTACATC TATATGCTAG CTCTTTAGTA TAAGTTGAA AAAGGGCCCC	780
	TTCTTGAGC ACATGGATAA AAGTATTATT GTAGCTAAA GATTGCTGGA TTGATATTGT	840
20	GTTGTTATAA TGAAGATAAG GTACACACTG AAACCACTGT CAGATTAGA AACTTCCACA	900
	ACTTGCTCA GTTCTTCAA CAATGGAGCA AGTTCCTTTT CTAGGCTGAC AATTAGTCCT	960
	GTATTGGCAC TGCTGCTGGC TATGAACTC ACCACCAAAG GTAAACGATT AAATTGAACC	1020
25	ACCTGGTAGG TGTATAGTA ACAGATGATA CTTTATTTT TGGAAAGTCC AAGTTTGCTT	1080
	CCTTGGTCTG TTGCAAGGC AAAAGTGGAT AAGAAACCAG GTCGCAAAGC ATGCTCTGGA	1140
	GCATTGTCAT TTGCCACTTT AATAACAGGT ACTCCATCTC TATCTGACAC AACAATGGCA	1200
30	TGGAGCCCTT CAACACTTGG TAACTTTTTA TACAAGAATC GCTTTAGGTC ATCCGCCATG	1260
	ATGAACCCCC TTCTCTCGCA GGATCAATCT CCACGCCTGG GGTTCCTGGG CTGCCTGGTT	1320
35	CTCTCCGCTG TCACTTCAGG GACAGCTTTA AAGACAGGTT CCTCCTCAAG CCACCGTCAC	1380
	ATGATTCATG ACCTCGTCTG CGCTCCAG	1408

40

(2) INFORMATION FOR SEQ ID NO: 50:

- 45 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1813 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

	CATGGTGGGG CACGAGATGG CCTCTRACTC TTCWAACACT TCACTGCCAT TCTCAAACAT	60
	GGGAAATCCA ATGAACACCA CACAGTTAGG GAAATCACIT TTTCAGTGGC AGGTGGAGCA	120
55	GGAAGAAAGC AAATTGGCAA ATATTTCCCA AGACCAGTTT CTTTCAAAGG ATGCAGATGG	180
	TGACACGTC CTTCATATTG CTGTTGCCCA AGGGAGAAGG GCACTTTCCT ATGTTCTTGC	240
60	AAGAAAGATG AATGCACTTC ACATGCTGGA TATTAAAGAG CACAATGGAC AGAGTGCCTT	300

TCAGGTGGCA GTGGCTGCCA ATCAGCATCT CATTGTGCAG GATCTGGTGA ACATCGGGGC 360  
ACAGGTGAAC ACCACAGACT GCTGGGGAAG AACACCTCTG CATGTGTGTG CTGAGAAGGG 420  
5 CCACTCCCAG GTGCTTCAGG CGATTTCAGAA GGGAGCAGTG GGAAGTAATC AGTTTGTGGA 480  
TCTTGAGGCA ACTAACTATG ATGGCCTGAC TCCCCTTCAC TGTGCAGTCA TAGCCCACAA 540  
10 TGCTGTGGTC CATGAACTCC AGAGAAATCA ACAGCCTCAT TCACCTGAAG TTCAGGAGCT 600  
TTTACTGAAG AATAAGAGTC TGGTTGATAC CATTAAAGTC CTAATTCAAA TGGGAGCAGC 660  
GGTGAAGCG AAGGATCGCA AAAGTGGCCG CACAGCCCTG CATTTGGCAG CTGAAGAAGC 720  
15 AAATCTGGAA CTCATTTCGCC TCTTTTGGGA GCTGCCCACTG TGCCTGTCTT TTGTGAATGC 780  
AAAGGCTTAC AATGGCAACA CTGCCCTCCA TGTTCCTGCC AGCTTGCAGT ATCGGTTGAC 840  
20 ACAATTAGAT GCTGTCCGCC TGTTCATGAG GAAGGGAGCA GACCCAAGTA CTCGGAACCT 900  
GGAGAACGAA CAGCCAGTGC ATTTGGTTCC CGATGGCCCT GTGGGAGAAC AGATCCGACG 960  
TATCCTGAAG GGAAAGTCCA TTCAGCAGAG AGCTCCACCG TATTAGCTCC ATTAGCTTGG 1020  
25 AGCCTGGCTA GCAACACTCA CTGTCAGTTA GGCAGTCCTG ATGTATCTGT ACATAGACCA 1080  
TTTGCCCTTAT ATTGGCAAAT GTAAGTTGTT TCTATGAAAC AAACATATTT AGTTCACATAT 1140  
30 TATATAGTGG GTTATATTAA AAGAAAAGAA RAAAAATATC TAATTWCTCT TGGCAGATTT 1200  
GCATATTTCA TACCCAGGTA TCTGGATCTA GACATCTGAA TTTGATCTCA ATGGTAACAT 1260  
TGCCCTCAAT TAACAGTAGC TTTTGAGTAG GAAAGGACTT TGATTGTGG CACAAAACAT 1320  
35 TATTAATATA GCTATTGACA GTTTCAAAGC AGGTAAATTG TAAATGTTTC TTTAAGAAAA 1380  
AGCATGTGAA AGGAAAAAGG TAAATACAGC ATTGAGGCTT CATTTGGCCT TAGTCCCTGG 1440  
40 GAGTTACTGG CGTTGGACAG GCTTCAGTCA TTGGACTAGA TGAAAGGTGT CCATGGTTAG 1500  
AATTTGATCT TTGCAAACTG TATATAATTG TTATTTTGT CTTAAAAAT ATTGTACATA 1560  
CTTGGTTGTT AACATGGTCA TATTTGAAAT GTATAAGTCC ATAAAATAGA AAAGAACAAG 1620  
45 TGAATTGTTG CTATTTAAAA AAATTTTACA ATTCTTACTA AGGAGTTTTT ATTGTGTAAT 1680  
CACTAAGTCT TTGTAGATAA AGCAGATGGG GAGTTACGGA GTTGTTCCTT TACTGGCTGA 1740  
50 AAGATATATT CGAATTGTAA AGATGCTTTT YTCATGCAT TGAAATTATA CATTATTTGT 1800  
AGGGAATTGC ATG 1813

55

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

60

(A) LENGTH: 2070 base pairs

(B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:	
	CCACGCGTCC GGAAGAGCGC GGCACCTCCG CTGGCCGCTG GCTCGCTGGC CGCTCCTGGA	60
10	GGCGGCGGCG GGAGCGCAGG GGGCGCGCGG CCCGGGGACT CGCATTCCCC GGTTCCTCCC	120
	CCACCCACG CGGCCTGGAC CATGGACGCC AGATGGTGGG CAGTGGTGGT GCTGGCTGGC	180
	TTCCCTCCC TAGGGGAGG TGGGAGACT CCCGAAGCCC CTCCGAGTC ATGGACCCAG	240
15	CTATGGTTCT TCCGATTGT GGTGAATGCT GCTGGCTATG CCAGCTTTAT GGTACCAGGC	300
	TACCTCCTGG TGCAGTACTT CAGGCGGAAG AACTACCTGG AGACCGGTAG GGGCCTCTGC	360
20	TTTCCCTGG TGAAAGCTTG TGTGTTTGGC AATGAGCCCA AGGCCTCTGA TGAGGTTCCT	420
	CTGGCGCCCC GAACAGAGGC GGCAGAGACC ACCCCGATGT GGCAGGCCCT GAAGCTGCTC	480
	TTCTGTGCCA CAGGGCTCCA GGTGTCTTAT CTGACTTGGG GTGTGCTGCA GGAAAGAGTG	540
25	ATGACCCGCA GCTATGGGGC CACAGCCACA TCACCGGGTG AGCGCTTTAC GGAATCGCAG	600
	TTCTGGTGC TAATGAACCG AGTGCTGGCA CTGATTGTGG CTGGCCTCTC CTGTGTTCTC	660
30	TGCAAGCAGC CCCGGCATGG GGCACCCATG TACCGGTACT CCTTTTGCCA GCCTGTCCAA	720
	TGTGCTTAGC AGCTGGTGCC AATACGAAGC TCTTAAGTTC GTCAGCTTCC CCACCCAGGT	780
	GCTGGCCAAG GCCTCTAAGG TGATCCCTGT CATGCTGATG GGAAAGCTTG TGTCTCGGCG	840
35	CAGTAACGAA CACTGGGAGT ACCTGACAGC CACCCTCATC TCCATTGGGG TCAGCATGTT	900
	TCTGCTATCC AGCGGACCAG AGCCCCGAG CTCCCCAGCC ACCACACTCT CAGGCCTCAT	960
40	CTTACTGGCA GGTATATATT CTTTGAACA GCTTCACCTC AAATGGCAG GATGCCCTGT	1020
	TTGCCTATAA GATGTCATCG GTGCAGATGA TGTTTGGGGG TCAATTTCTT CTCCTGCCTC	1080
	TTACAGTGG GCTCACTGCT AGAAACAGGG GGCCCTACTG GAGGGAACCC GCTTCATGGG	1140
45	GCGACACAGT GAGTTTGCTG CCCATGCCCT GCTACTCTCC ATCTGCTCCG CATGTGGCCA	1200
	GCTCTTCATC TTTTACACCA TTGGGCAGTT TGGGGCTGCC GTCTTCACCA TCATCATGAC	1260
50	CCTCCGCCAG GCCTTTGCCA TCCTTCTTTC CTGCCTTCTC TATGGCCACA CTGTCACTGT	1320
	GGTGGGAGGG CTGGGGGTGG CTGTGGTCTT TGCTGCCCTC CTGCTCAGAG TCTACGCGCG	1380
	GGGCCGTCTA AAGCAACGGG GAAAGAAGGC TGTGCCTGTT GAGTCTCTTG TGCAGAAGGT	1440
55	TTGAGGGTGG AAAGGGCCTG AGGGGTGAAG TGAAATAGGA CCCTCCCACC ATCCCTTCT	1500
	GCTGTAACTT CTGAGGAGC TGGCTGAAAG GGCAAAATGC AGGTGTTTTT TCAGTATCAC	1560
60	AGACCAGCTC TGCAGCAGGG GATTGGGGAG CCCAGGAGGC AGCCTTCCCT TTTGCCTTAA	1620

GTCACCCATC TTCCAGTAAG CAGTTTATTC TGAGCCCCGG GGGTAGACAG TCCTCAGTGA 1680  
 GGGGTTTGGG GGAGTTTGGG GTCAAGAGAG CATAGGTAGG TTCCACAGTT ACTCTTCCCA 1740  
 5 CAAGTTCCTT TAAGTCTTGC CCTAGCTGTG CTCTGCCACC TTCCAGACTC ACTCCCCTCT 1800  
 GCAAATACCT GCATTTCTTA CCCTGGTGAG AAAAGCACAA GCGGTGTAGG CTCCAATGCT 1860  
 10 GCTTTCCCAG GAGGGTGAAG ATGGTGCTGT GCTGAGGAAA GGGGATGCAG AGCCCTGCC 1920  
 AGCACCACCA CCTCCTATGC TCCTGGATCC CTAGGCTCTG TTCCATGAGC CTGTTGCAGG 1980  
 TTTTGGTACT TTAGAAATGT AACTTTTTCG TCTTATAATT TTATTTTATT AAATTAAATT 2040  
 15 ACTGCAAAAA AAAAAAAAAA AAAAAAAAAA 2070

20 (2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1426 base pairs

(B) TYPE: nucleic acid

25 (C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

30 CCCTCACTAA AGGGAACAAA AGCTGGAGCT CCACCGCGGT GGCGGCCGCT CTAGAACTAG 60  
 TGGATCCCCC GGGCTGCAGG AATTCGGCAC ACGGATCGGC GTCCGCAGCG GGCGGCTGCT 120  
 GAGCTGCCTT GAGGTGCAGT GTTGGGGATC CAGAGCCATG TCGGACCTGC TACTACTGGG 180  
 35 CCTGATTGGG GGCCTGACTC TCTTACTGCT GCTGACGCTG CTGGCCTTTG CCGGGTACTC 240  
 AGGGCTACTG GCTGGGGTGG AAGTGAGTGC TGGGTACCC CCCATCCGCA ACGTCACTGT 300  
 40 GGCTTACAAG TTCCACATGG GGCTCTATGG TGAGACTGGG CGGCTTTTCA CTGAGAGCTG 360  
 CAGCATCTCT CCAAGCTCC GCTCCATCGC TGTCTACTAT GACAACCCCC ACATGGTGCC 420  
 CCCTGATAAG TGCCGATGTG CCGTGGGCAG CATCCTGAGT GAAGGTGAGG AATCGCCCTC 480  
 45 CCCTGAGCTC ATCGACCTCT ACCAGAAATT TGGCTTCAAG GTGTTCTCCT TCCCGGAACC 540  
 CAGCCATGTG GTGACAGCCA CCTTTCCCCT AACACCACCA TTCTGTCCCA TCTGGCTGGG 600  
 50 CTACCCGCCG TGTCATCCT GCCTTGACA CCTACATCAA GGAGCGGAAG CTGTGTGCCT 660  
 ATCTCGGCT GSGATCTAC CAGGAAGACC AGAATCCATT TCATGTGCCC ACTGGCACGG 720  
 CCAGGGAGAC TTCTATGTGC CTGAGATGAA GGAGACAGAG TGGAAATGGC GGGGGCTTGT 780  
 55 GGAGGCCATT GACACCCAGG TGGATGGCAC AGGAGCTGAC ACAATGAGTG ACACGAGTTC 840  
 TGTAAGCTTG GAAGTGAGCC CTGGCAGCCG GGAGACTTCA GCTGCCACAC TGTCACCTGG 900  
 60 GCGGAGCAGC CGTGGCTGGG ATGACGGTGA CACCCGAGC GAGCACAGCT AACAGCGAGT 960

CAGGTGCCAG CGGCTCCTCT TTTGAGGAGC TGGACTTTGG AGGGCGAGGG GCCCTTAAGG 1020  
 5 GGAGTCACGG CTGGACCCTG GGACTTGAGC CCCTGGGGGA CTACCAAGTG GCTCTGGGAG 1080  
 CCCACTGCCC CTGAGAAGGG CAAGGAGTAA CCCATGGCCT GCACCCTCCT GCAGTGCAGT 1140  
 TGCTGAGGAA CTGAGCAGAC TCTCCAGCAG ACTCTCCAGC CCTCTTCCTC CTTCCTCTGG 1200  
 10 GGGAHGAGGG GTTCCTGAGG GACCTGACTT CCCCTGCTCC AGGCCTCTTG CTAAGCCTTC 1260  
 TCCTCACTGC CCTTTAGGCT CCCAGGGCCA GAGGAGCCAG GGACTATTTT CTGCACCAGC 1320  
 CCCCAGGGCT GCCGCCCTG TTGTGTCTTT TTTTCAGACT CACAGTGGAG CTTCCAGGAC 1380  
 15 CCAGAATAAA GCCAATGATT TACTTGTTAA AAAAAAAAAA AAAAAA 1426

20

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1720 base pairs  
 25 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

GGCACGAGTG CGGCCCCAGC CTCTCCTCAC GTCGCGCAG TCTCCGCCGC AGTCTCAGCT 60  
 GCAGCTGCAG GACTGAGCCG TGCACCCGGA GGAGACCCCC GGAGGAGGCG ACAAACTTCG 120  
 35 CAGTGCCGCG ACCCAACCCC AGCCCTGGGT AGCCTGCAGC ATGGCCCAGC TGTTCCTGCC 180  
 CCTGCTGGCA GCCCTGGTCC TGGCCCAGGC TCCTGCAGCT TTAGCAGATG TTCTGGAAGG 240  
 AGACAGCTCA GAGGACCGCG CTTTTCGCGT GCGCATCGCG GCGACGCGC CACTGCAGGG 300  
 40 CGTGCTCGGC GCGGCCCTCA CCATCCCTTG CCACGTCCAC TACCTGCGGC CACCGCCGAG 360  
 CCGCCGGGCT GTGCTGGGCT CTCCGCGGGT CAAGTGGACT TTCCTGTCCC GGGGCCGGGA 420  
 45 GGCAGAAGTG CTGGTGGCGG GGGGAGTGCG CGTCAAGGTG AACGAGGCCT ACCGGTTCCG 480  
 CGTGGCACTG CTGCGTACC CAGCGTCGCT CACCGACGTC TCCCTGGCG CTGAGCGAGC 540  
 TGCGCCCCAA CGACTCAGGT ATCTATCGCT GTGAGGTCCA GCACGGCATC GATGACAGCA 600  
 50 GCGACGCTGT GGAGGTCAAG GTCAAAGTA TCCCATCCAG ACCCCACGAG AGGCCTGTTA 660  
 CGGAGACATG GATGGCTTCC CCGGGGTCGG GAACTATGGT GTGGTCCACC CGGATGACCT 720  
 55 CTATGATGAG TACTGTTATG CTGAAGACCT AAATGGAGAA CTGTTTCCTG GTGACCCTCC 780  
 AGAGAAGCTG ACATTGGAGG AAGCACGGGC GTACTGCCAG GAGCGGGGTG CAGAGATTGC 840  
 CACCACGGGC CAACTGTATG CAGCCTGGGA TGGTGGCCTG GACCACTGCA GCCCAGGGTG 900  
 60

GCTAGCTGAT GGCAGTGTGC GCTACCCCAT CGTCACACCC AGCCAGCGCT GTGGTGGGGG 960  
 CTTCCTGGT GTCAAGACTC TCTTCCTCTT CCCCAACCAG ACTGGCTTCC CCAATAAGCA 1020  
 5 CAGCCGCTTC AACGTCTACT GCTTCCGAGA CTCGGCCCAG CTTCTGCCAT CCCTGAGGCC 1080  
 TCCAACCCAG COTCCAACCC AGCTTTGATG GACTAGAGGC TATCGTCACA GTGACAGAGA 1140  
 10 CCCTGGAGGA ACTGCAGCTG CCTCAGGAAG CCACAGAGAG TGAATCCCGT GGGGCCATCT 1200  
 ACTCCATCCC CATCATGGAG GACGGAGGAG GTGGAAGCTC CACTCCAGAA GACCCAGCAG 1260  
 AGGCCCTAG GACGCTCCTA GAATTTGAAA CACAATCCAT GGTACCGCCC ACGGGGTCTT 1320  
 15 CAGAAGAGGA AGGTAAGGCA TTGGAGGAAG AAGAGAAATA TGAAGATGAA GAAGAGAAAG 1380  
 AGGAGGAAGA AGAAGAGGAG GAGGTGGAGG ATGAGGCTCT GTGGGCATGG CCCAGCGAGC 1440  
 TCAGCAGCCC GGGCCCTGAG GCCTCTCTCC CCACTGAGCC AGCAGCCCAG GAGGAGTCAC 1500  
 20 TCTCCAGGC GCCAGCAAGG GCAGTCCTGC AGCCTGGTGC ATCACCCTT CCTGATGGAG 1560  
 AGTCAGAAGC TTCCAGGCCT CCAAGGGTCC ATGGACCACC TACTGAGACT CTGCCCACTC 1620  
 25 CCAGGGAGAG GAACCTAGCA TCCCCTAC CTTCCACTCT GGTGAGGCA AGAGAGGTGG 1680  
 GGGAGGCAAC TGGTGGTCCT GAGCTATCTG GGTCCCTCGA 1720

30

(2) INFORMATION FOR SEQ ID NO: 54:

35 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1117 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

GGACAGAGGC CAAACTTCGG GCGGCTGAGG CGGCGGCCGA GGAGCGGCGG ACTCCGGGCG 60  
 CGGGGAGTCG AGGCATTTGC GCCTGGGCTT CGGAGCGTAC CCAGGGCCTG AGCCTTTGAA 120  
 45 GCAGGAGGAG GGGAGGAGAG AGTGGGGCTC CTCTATCGGG ACCCCCTCCC CATGTGGATC 180  
 TGCCCAGGCG GCGGCGGCGG AGGAGGCGAC CGAGAAGATG CCCGCCCTGC GCCCCGCTCT 240  
 50 GCTGTGGGCG CTGCTGGCGC TCTGGCTGTG CTGCGCGACC CCCGCGCATG CATTGCAGTG 300  
 TCGAGATGGC TATGAACCCT GTGTAAATGA AGGAATGTGT GTTACCTACC ACAATGGCAC 360  
 AGGATACTGC AAAGTCCAG AAGGCTTCTT GGGGAATAT TGTCAACATC GAGACCCCTG 420  
 55 TGAGAAGAAC CGCTGCCAGA ATGGTGGGAC TTGTGTGGCC CAGGCCATGC TGGGGAAGC 480  
 CACGTGCCGA TGTGCCTCAG GGTTFACAGG AGAGGACTGC CAGTACTCGA CATCTCATCC 540  
 60 ATGCTTTGTG TCTCGACCTT GCCTGAATGG CGGCACATGC CATATGCTCA GCCGGGATAC 600

CTATGAGTGC ACCTGTCAAG TCGGGTTTAC AGGTAAGGAG TGCCAATGGA CCGATGCCTG 660  
 CCTGTCTCAT CCCTGTGCAA ATGGAAGTAC CTGTACCACT GTGGCCAACC ATTTCTCTGCA 720  
 5 AATGCCTCAC AGGCTTCACA GGGCAGAAGT GTGAGACTGA TGTCAATGAG TGTGACATTC 780  
 CAGGACACTG CCAGCATGGT GGCACCTGCC TCAACCTGCC TGGTTCCTAC CAGTGCCAGT 840  
 10 GCCTTCAGGG CTTACAGGC CAGTACTGTG ACAGCCTGTA TGTGCCCTGT GCACCCTCGC 900  
 CTTGTGTCAA TGGAGGCACC TGTGGCAGA CTGGTGACTT CACTTTTGAG TGCAACTGCC 960  
 TTCCAGAAAC AGTGAGAAGA GGAACAGAGC TCTGGGAAAG AGACAGGGAA GTCTGGAATG 1020  
 15 GAAAAGAACA CGATGAGAAT TAGACACTGG AAAATATGTA TGTGTGGTTA ATAAAGTGCT 1080  
 TTAAACTGAA AAAAAAAAAA AAAAAAAAAA AAAAAA 1117  
 20

## (2) INFORMATION FOR SEQ ID NO: 55:

25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1903 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

GGCACGAGCT CGGAGAGGCG GCGCCCTGA GTAGGCCAGG AGCCTCTCTT GCAACTTCTG 60  
 35 CCACCGCGGG CCACCGCGGC CGCCTGATCC CGCAGAGGAA GGTCGCGGCC GTGGAGCGAT 120  
 GACCCGCGGC GGTCCGGGCG GCGCCCGGG GCTGCCACAG CCGCCGCCGC TTCTGCTGCT 180  
 40 GCTGCTGCTG CCGCTGTTGT TAGTCACCGC GGAGCCGCCG AAACCTGCAG GAGTCTACTA 240  
 TGCAACTGCA TACTGGATGC CTGCTGAAAA GACAGTACAA GTCAAAAATG TAATGGACAA 300  
 GAATGGGGAC GCCTATGGCT TTTACAATAA CTCTGTGAAA ACCACAGGCT GGGGCATCCT 360  
 45 GGAGATCAGA GCTGGCTATG GCTCTCAAAC CCTGAGCAAT GAGATCATCA TGTTTGTGGC 420  
 TGGCTTTTGT GAGGGTTACC TCATTGCCCC ACACATGAAT GACCACTACA CAAACCTCTA 480  
 CCCACAGCTG ATCACGAAAC CTTCCATCAT GGATAAAGTG CAGGATTTTA TGGAGAAGCA 540  
 50 AGATAAGGTG GACCCGAAA AATATCAAAG AATACAAGAC TGATTCAITT TGGAGACATA 600  
 CAGGCTATGT GATCGCACAA ATAGATGGCC TCTATGTAGG AGCAAAAGAAG AGGGCTATAT 660  
 55 TAGAAGGGAC AAAGCCAATG ACCCTGTTCC AGATTCAAGT CCTGAAATAGT GTTGGAGATC 720  
 TATTGGATCT GATTCCCTCA CTCTCTCCCA CAAAAACGG CAGCCTAAAG GTTTTAAAGA 780  
 60 GATGGGACAT GGGACATTGC TCCGCTCTTA TCAAGGTTCT TCCTGGATTG GAGAACATCC 840

	TTTTTGCTCA CTCAAGCTGG TACACGTATG CAGCCATGCT CAGGATATAT AAACACTGGG	900
	ACTTCAACAT CATAGATAAA GATACCAGCA GTAGTCGCCT CTCTTTCAGC AGTTACCCAG	960
5	GGTTTTTGGA GTCTCTGGAT GATTTTTTACA TTCTTAGCAG TGGATTGATA TTGCTGCAGA	1020
	CCACAAACAG TGTGTTTAAT AAAACCCCTGC TAAAGCAGGT AATACCCGAG ACTCTCCTGT	1080
10	CCTGGCAAAG AGTCCGTGTG GCCAATATGA TGGCAGATAG TGGCAAGAGG TGGGCAGACA	1140
	TCTTTTCAAA ATACAACCTCT GGCACCTATA ACAATCAATA CATGGTCTTG GACCTGAAGA	1200
	AAGTAAAGCT GAACCACAGT CTTGACAAAG GCACTCTGTA CATTGTGGAG CAAATTCCCTA	1260
15	CATATGTAGA ATATTCTGAA CAACTGATG TTCTACGGAA AGGATATTGG CCCTCCTACA	1320
	ATGTTCCCTTT CCATGAAAAA ATCTACAACCT GGAGTGGCTA TCCACTGTTA GTTCAGAAGC	1380
	TGGGCTTGGA CTACTCTTAT GATTTAGCTC CACGAGCCAA AATTTTCCGG CGTGACCAAG	1440
20	GGAAAGTGAC TGATACGGCA TCCATGAAAT ATATCATGCG ATACAACAAT TATAAGAAGG	1500
	ATCCTTACAG TAGAGGTGAC CCCTGTAATA CCATCTGCTG CCGTGAGGAC CCTGAACCTCA	1560
25	CCTAACCCAA GTCCTTGGAG GTTGTATTGA CACAAAAGGT GGCAGATATY TACCTAGCAT	1620
	CTCAGTACAC ATCCTATGCC ATAAGTGGTC CCACAGTACA AGGTGGCCTC CCTGTTTTTTC	1680
	GCTGGGACCG TTTCAACAAA ACTCTACATC AGGGCATGCC AGAGGTCTAC AACTTTGATT	1740
30	TTATTACCAT GAAACCAATT TTGAAACTTG ATATAAAATG AAGGAGGGAG ATGACGGACT	1800
	AGAAGACTGT AAATAAGATA CCAAAGGCAC TATTTTAGCT ATGTTTTTCC CATCAGAAAT	1860
35	ATGCAATAAA ATATATTAAT TTGTCAAAAA AAAAAAAAAA AAA	1903

40 (2) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 1869 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

50	ACAGCTTTTC GGGCCCCGAG TCGCACCCAG CGAAGAGAGC GGGCCCCGGA CAAGCTCGAA	60
	CTCCGGCCGC CTGCCCCTTC CCCGGCTCCG CTCCCTCTGC CCCCTCGGGG TCGCGCGCCC	120
	ACGATGCTGC AGGGCCCTGG CTCGCTGCTG CTGCTCTTCC TCGCCTCGCA CTGCTGCCTG	180
55	GGCTCGGCGC GCGGGCTCTT CCTCTTTGGC CAGCCCGACT TCTCCTACAA GCGCANCAAT	240
	TGCAAGCCCA TCCCGGTCAA CCTGCAGCTG TGCCACGGCA TCGAATACCA GAACATGCGG	300
60	CTGCCCAACC TGCTGGGCCA CGAGACCATG AAGGAGGTGC TGGAGCAGGC CGGCGCTTGG	360



ATCCCGCTGG TCATGAAGCA GTGCCACCCG GACACCAAGA AGTTCCTGTG CTCGCTCTTC 420  
 5 GCCCCCGTCT GCCTCGATGA CCTAGACGAG ACCATCCAGC CATGCCACTC GCTCTGCGTG 480  
 CAGGTGAAGG ACCGCTGCGC CCCGGTCAATG TCCGCCTTCG GYTTCCCTTG GCCCGACATG 540  
 CTTGAGTGCG ACCGTTTCCC CCAGGACAAC GACCTTTGCA TCCCCCTCGC TAGCAGCGAC 600  
 10 CACCTCCTGC CAGCCACCGA GGAAGCTCCA AAGGTATGTG AAGCCTGCAA AAATAAAAAT 660  
 GATGATGACA ACGACATAAT GGAAACGCTT TGTAAAAATG ATTTTGCACT GAAAAATAAA 720  
 15 GTGAAGGAGA TAACCTACAT CAACCGAGAT ACCAAAATCA TCCTGGAGAC CAAGAGCAAG 780  
 ACCATTTACA AGCTGAACGG TGTGTCCGAA AGGGACCTGA AGAAATCGGT GCTGTGGCTC 840  
 AAAGACAGCT TGCAGTGAC CTGTGAGGAG ATGAACGACA TCAACGCGCC CTATCTGGTC 900  
 20 ATGGGACAGA AACAGGGTGG GGAGCTGGTG ATCACCTCGG TGAAGCGGTG GCAGAAGGGG 960  
 CAGAGAGAGT TCAAGCGCAT CTCCCGCAGC ATCCGCAAGC TGCAGTGCTA GTCCCGGCAT 1020  
 CCTGATGGCT CCGACAGGCC TGCTCCAGAG CACGGCTGAC CATTTCTGCT CCGGGATCTC 1080  
 25 AGCTCCCGTT CCCCAAGCAC ACTCCTAGCT GCTCCAGTCT CAGCCTGGGC AGCTTCCCCC 1140  
 TGCCTTTTGC ACGTTTGCAT CCCCAGCATT TCCTGAGTTA TAAGGCCACA GGAGTGGATA 1200  
 30 GCTGTTTTCA CCTAAAGGAA AAGCCCACCC GAATCTTGTA GAAATATTCA AACTAATAAA 1260  
 ATCATGAATA TTTTTATGAA GTTTAAAAAT AGCTCACTTT AAAGCTAGTT TTGAATAGGT 1320  
 35 GCAACTGTGA CTGGGGTCTG GTTGGTTGTT GTTTGTTGTT TTGAGTCAGC TGATTTTCAC 1380  
 TTCCCACTGA GGTGTGCATA ACATGCAAAT TGCTTCAATT TTCTCTGTGG CCCAAACTTG 1440  
 TGGGTCACAA ACCCTGTTGA GATAAAGCTG GCTGTTATCT CAACATCTTC ATCAGCTCCA 1500  
 40 GACTGAGACT CAGTGTCTAA GTCTTACAAC AATTCATCAT TTTATACCTT CAATGGGAAC 1560  
 TTAAACTGTT ACATGTATCA CATTCCAGCT ACAATACTTC CATTATTAG AAGCACATTA 1620  
 45 ACCATTCTTA TAGCATGATT TCTTCAAGTA AAAGGCAAAA GATATAAATT TTATAATTGA 1680  
 CTTGAGTACT TTAAGCCTTG TTAAAAACAT TTCTTACTTA ACTTTTGCAA ATTAAACCCA 1740  
 TTGTAGCTTA CCTGTAATAT ACATAGTAGT TTACCTTTAA AAGTTGTAAA AATATTGCTT 1800  
 50 TAACCAACAC TGTAATATTT TCAGATAAAC ATTATATTCT TGTATATAAA CTTTACATCC 1860  
 TGTTTTACC 1869

55

(2) INFORMATION FOR SEQ ID NO: 57:

60

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1259 base pairs

(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

	ACCGTGGTCG TGGGCGGACG GCGGCTGCAG CGYGGAGGAG CTGGGGTCGC TGTGGGTCGC	60
10	GAACAGAGCC CGGGACGTGC GCGCTTGGTG CACGATCCTG AAGGGGAGCT CCGAGGGGCC	120
	CGGGTCKCCA GGGCTGCTGC GGCCATTCCC GGAGCCCGGC GCGGGGCCCG NRAGATACTG	180
	GTTTAGGCCG TCCCAGGGCT CCGGGCGCAC CCGKTGGCCG CTGCTGCAGC GGAGGGAGCG	240
15	CGGCGGCGSG NGGGCTCGGA GACAGCGTTT CTCCCGGAAT CTTCTCGGG CAGCARGTGG	300
	GAAGTGGGAG CCGGAGCGGC ACTGGCARGC TTCTCTCCGC ANGTCGGCAC CATGCGCCCT	360
20	GCAGCCCTGC GCGGGGCCCT GCTGGGCTGC CTCTGCCTGG CGTTGCTTTG CCTGGGCGGT	420
	GCGGACAAGC GCCTGCGTGA CAACCATGAG TGGAAAAAC TAATTATGGT TCAGCACTGG	480
	CCTGAGACAG TATGCGAGAA AATTCAAAAC GACTGTAGAG ACCCTCCGGA TTACTGGACA	540
25	ATACATGGAC TATGGCCCGA TAAAAGTGAA GGATGTAATA GATCGTGGCC CTTCAATTTA	600
	GAAGAGATTA AGGATCTTTT GCCAGAAATG AGGGCATACT GGCCTGACGT AATTCACG	660
30	TTTCCCAATC GCAGCCGCTT CTGGAAGCAT GAGTGGGAAA AGCATGGGAC CTGCGCCGCC	720
	CAGGTGGATG CGCTCAACTC CCAGAAGAAG TACTTTGGCA GAAGCCTGGA ACTCTACAGG	780
	GAGCTGGACC TCAACAGTGT GCTTCTAAAA TTGGGGATAA AACCATCCAT CAATTACTAC	840
35	CAAGTTGCAG ATTTTAAAGA TGCCCTTGCC AGAGTATATG GAGTGATACC CAAAATCCAG	900
	TGCCTTCCAC CAAGCCAGGA TGAGGAAGTA CAGACAATTG GTCAGATAGA ACTGTGCCTC	960
40	ACTAAGCAAG ACCAGCAGCT GCAAACTGC ACCGAGCCGG GGGAGCAGCC GTCCCCAAG	1020
	CAGGAAGTCT GGCTGGCAAA TGGGGCCGCC GAGAGCCGGG GTCTGAGAGT CTGTGAAGAT	1080
	GGCCCAGTCT TCTATCCCC ACCTAAAAAG ACCAAGCATT GATGCCCAAG TTTTGGAAT	1140
45	ATTCTGTTTT AAAAAGCAAG AGAAATTCAC AAACTGCAGC TTTCTNAAAA AAAAANAAAA	1200
	AAAAATTGGG GGGTTTTTTT GGGSGCCCG GGGCCCTTGG TTTTCCCCC CGGGGGGT	1259

50

(2) INFORMATION FOR SEQ ID NO: 58:

55 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 1186 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

	CGGCATGGAG AATGGCTCCG CTTCTGTTGC AGCTGGCGGT GCTCGGCGCG GCGCTGGCGG	60
5	CCGCAGCCCT CGTACTGATT TCCATCGTTG CATTTACAAC TGCTACAAAA ATGCCAGCAC	120
	TCCATCGACA TGAAGAAGAG AAATTCCTTCT TAAATGCCAA AGGCCAGAAA GAAACTTTAC	180
	CCAGCATATG GGAATCACCT ACCAAACAAC TTCTGTCTGT TGTGCCTTCA TACAATGAAG	240
10	AAAAACGGTT GCCTGTGATG ATGGATGAAG CTCTGAGCTA TCTAGAGAAG AGACAGAAAC	300
	GAGATCCTGC GTTCACTTAT GAAGTGATAG TAGTTGATGA TGGCAGTAAA GATCAGACCT	360
15	CAAAGGTAGC TTTTAAATAT TGCCAGAAAT ATGGAAGTGA CAAAGTACGT GTGATAACCC	420
	TGGTGAAGAA TCGTGGAAAA GGTGGAGCGA TTAGAATGGG TATATTCACT TCTCGAGGAG	480
	AAAAGATCCT TATGGCAGAT GCTGATGGAG CCACAAAGTT TCCAGATGTT GAGAAATTAG	540
20	AAAAGGGGCT AAATGATCTA CAGCCTTGGC CTAATCAAAT GGCTATAGCA TGTGGATCTC	600
	GAGCTCATTT AGAAAAAGAA TCAATTGCTC AGCGTTCTTA CTTCCGTACT CTTCTCATGT	660
25	ATGGGTTCCTA CTTTCTGGTG TGGTTCCTTT GTGTCAAAGG AATCAGGGAC ACACAGTGTG	720
	GGTTCAAATT ATTTACTCGA GAAGCAGCTT CACGGACGTT TTCATCTCTA CACGTTGAAC	780
	GATGGGCATT TGATGTAGAA CTAATGTACA TAGCACAGTT CTTTAAATTT CCAATAGCAG	840
30	AAATTGCTGT CAACTGGACA GAAATGAAG GTTCTAAATT AGTTCCATTC TGGAGCTGGC	900
	TACAAATGGG TAAAGACCTA CTTTTTATAC GACTTCGATA TTTGACTGGT GCCTGGAGGC	960
35	TTGAGCAAAC TCGGAAAATG AATTAGGTTG TTTCAGTCT TCAGTTGTGT TCTTATGCTT	1020
	CAGTGTACACA TTTCATTTCA TTTGAACTA AAATTTTAAG TAAAGCTGAA ATAACTTTCT	1080
	TGTCATTGTC TGCCTTTTGA TAATTTTAAA GAAATAACTT TCCATAAGTA AAAAATTATA	1140
40	TATCTCTTTG GATATAAATG ATTTTAAAA GATGTTTATT TAAAAA	1186

45 (2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

- 50 (A) LENGTH: 428 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

55	GATCCCQCGG CTGCAGGATT CGGCACGAGT ACTGATTCTT CACTGAGCTT KGTAGTATA	60
	AGCAGAGTTC CAAGTCTCCC CTAGGGTTGT CTCTACATTT CTTTATCATT CCAGTGGGTA	120
60	RGTTTAGCT GGGGGAAGGA CATTTTATAA GGGTTAGTTG GACTGAGCAG TATGGACATT	180

TGCTTTTTC ATTACGTACT GTTGTTTTTC CTGTGTTAGGT GTGCTTTGGT GGTTTTAATA 240  
 TTATTGTGCC AGGGATGGGG AAATGGGGGG GGTGTGTGG GAAGAGTACT TATTATGTG 300  
 5 TTTTCTTCAG TGTAAATGTT CTTGGTAATT GATACCTCTC TGTTTTATTT NTCTCATCT 360  
 TTCAAAATAA AACTTTTTGA AATTTGAAAA AAAAAAAAAA NAAAAAACTC GGGGGGGGGC 420  
 CCGGTACC 428  
 10

15 (2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 501 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 20 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:  
 25 GGCACGAGCT TTCAGCAGGG GACAGCCCGA TTGGGGACAA TGGCGTCTCT TGGCCACATC 60  
 TTGGTTTTCT GTGTGGGTCT CCTCACCATG GCCAAGGCAG AAAGTCCAAA GGAACACGAC 120  
 CCGTTCACCTT ACGACTACCA GTCCCTGCAG ATCGGAGGCC TCGTCATCGC CGGGATCCTC 180  
 30 TTCATCCTGG GCATCCTCAT CGTGCTGAGC AGAAGATGCC GGTGCAAGTT CAACCAGCAG 240  
 CAGAGGACTG GGGAAACCCGA TGAAGAGGAG GGAACCTTCC GCAGCTCCAT CCGCCGCTCG 300  
 TCCACCCGCA GCGCGTAGAA ACACCTGGAG CGATGGAATC CGGCCAGGAC TCCCCTGGCA 360  
 35 CCTGACATCT CCCACGCTCC AACTGCGCGC CCACCGCCCC CTCCGCGGCC CCTTCCCCAG 420  
 CCCTGCCCCC GCAGACTCCC CCTGCGGCCA AGACTTCCAA TAAAACGTGC GTTCCTCTCG 480  
 40 AAAAAAAAAA AAATAAAAAA A 501

45 (2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1197 base pairs  
 (B) TYPE: nucleic acid  
 50 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:  
 55 ACATGATGGN TACCAAAGAA TTCGGCANAG GGCGCGCAGT GCAGCAGGTG CTCAATATCG 60  
 AGTGCCCTGCG GGACTTCCTG ACGCCCCCGC TGCTGTCCGT GCGCTTCCGG TACGTGGGCG 120  
 CCCCCAGGC CCTCACCTG AAGCTCCCAG TGACCAKCAA CAAGTTCTTC CAGCCCACCG 180  
 60

207

	AGATGGCGGC CCAGGATTTC TTCCAGCGCT GGAAGCAGCT GAGCCTCCCT CAACAGGAGG	240
	CGCAGAAAAT CTTCAAAGCC AACCACCCCA TGGACGCAGA AGTTACTAAG GCCAAGCTTC	300
5	TGGGGTTTGG CTCTGCTCTC CTGGACAATG TGGACCCCAA CCCTGAGAAC TTCGTGGGGG	360
	CGGGGATCAT CCAGACTAAA GCCCTGCAGG TGGGCTGTCT GCTTCGGCTG GAGCCCAATG	420
10	CCCAGGCCCA GATGTACCGG CTGACCCTGC GCACCAGCAA GGAGCCCGTC TCCCGTCACC	480
	TGTGTGAGCT GCTGGCACAG CAGTTCTGAG CCCTGGACTC TGCCCCGGGG GATGTGGCCG	540
	GCACTGGGCA GCCCCTTGGA CTGAGGCAGT TTTGGTGGAT GGGGGACCTC CACTGGTGAC	600
15	AGAGAAGACA CCAGGGTTTG GGGGATGCCT GGGACTTTCC TCCGGCCTTT TGTATTTTTA	660
	TTTTTGTTCA TCTGCTGCTG TTTACATTCT GGGGGGTTAG GGGGAGTCCC CCTCCCTCCC	720
	TTTCCCCCCC AAGCACAGAG GGGAGAGGGG CCAGGGAAGT GGATGTCTCC TCCCCTCCCA	780
20	CCCCACCTG TTGTAGCCCC TCCTACCCCC TCCCCATCCA GGGGCTGTGT ATTATTGTGA	840
	GCGAATAAAC AGAGAGACGC TAACAGCCCC ATGTCTGTGT CCATCACCCA CTGTTAGGTA	900
25	GTCAAAGAAG TGGGGTGAGG GCATGCAGAG TGTGGGTGGC CAGNTTCGCA GCCCATGGGT	960
	GGGACTCTGG GGAGACAGCA GCAGCAGCAG CCGCCGAAGC CCCAGCTGCA AGGCCACCAG	1020
	ACGCACTCCT GTGCCTGGTT CETYAGTCCC CAACACCAGG TAGCAAGCTY TGGGCAGCTG	1080
30	GGCCTGGTAG ACCTCATCTT CTGTCTTCTY TGGTGGCCCT GGCTCTGGTG GGAAGTGCCT	1140
	GGAGGTGACC AGGGTATAGA AGTTTCGGAG CTGATTGGAA GAGGATTAAC TTCCCGC	1197
35		

## (2) INFORMATION FOR SEQ ID NO: 62:

40	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 595 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: linear	
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:	
	ATTNANGACK TKYAGCCTYT WATACMATCA TTATAGGGAR AAGCTGGTAC GCCTGMARGT	60
50	ACCGGTCYGG AATTCNCGGG TCGACCCACG CGTCCGGCAC AGCGGGAGTT GGTCTGACA	120
	CCAGATGTTT TCTGCTCCTG GTTAATGTCA GTGAGGGCTG GAAGTTGAAT AAATGAGAAC	180
55	AGGAGTGGTC TGGGCCCCATG TAAATGATCC TCCCTTGAAA GGAGGAACAG CTTTCATCAT	240
	TTGTTCACG TAAGCCTTGC ATGCATTATA GATCTGGTGC TAAGCAGTGG GAAAGATCTC	300
	ATAAGTAATG TTTTATGTTT TTTCTGTCTC TCCTCTTCTG TWGTTCTTGG CTTGTGGGTT	360
60	GTGTTTGTGT GTTAACTGGA AAATTGCTAT AAGCCAGTTG TCTCTAAGTT TTAAAAACGA	420

ATTAGAAAA CCATAAATC TCTGGCCTAT GCACATGTGC CCTGTTTGTG TAAAACATTA 480  
 AAGGGTAAAT AAAAAGGAAG GAGAACAGTC AATAATGTGC ATCAAATATA TTCTGAGTTC 540  
 5 TAGAGAAATT AATGACCAAG CATTAGAACT AGAAGCAAAA AAAAAAAAAA AAAAA 595

10

(2) INFORMATION FOR SEQ ID NO: 63:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1478 base pairs  
 15 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

20 CGGCGCTGAG GACGCACGGA TGCCTTCCGT GCCTTCCATC AAGATCTCAA TTTGTGCGC 60  
 AAGTTCCTAC AGCCCTGTGT GATTGGAGAG CTGGTCCGG AAGAACCAG CCAGGATGA 120  
 25 CCCCTGAATG CGCATGGTCG AGGACTTCCG AGCCCTGCAC CAGGCAGCCG AGGACATGAA 180  
 GCTGTTTGAT GCCAGTCCCA CCTTCTTTGC TTTCTACTG GGCCACATCC TGGCCATGA 240  
 GGTGCTGGCC TGGCTCCTTA TCTACCTCCT GGGTCTGGC TGGGTGCCA GTGCCCTGGN 300  
 30 CCGCCTTCAT CCTGGCCATC TCTCAGGCTC AGTCTGGTG TCTGCAGCAT GACCTGGGCC 360  
 ATGCTCCATC TTCAAGAAGW CCTGGTGGAA CCACGTGGC CAGAAGTTCG TGATGGGGCA 420  
 35 GCTAAAGGGC TTCTCCGCCC ACTGGTGGAA CTTCGCCAC TTCCAGCACC ACGCCAAGCC 480  
 CAACATCTTC CACAAAGACC CAGACGTGAC GGTGGCGCCC GTCTTCCTCC TGGGGGAGTC 540  
 ATCCGTCGAG TATGGCAAGA AGAAACGCAG ATACCTACCC TACAACCAGC AGCACCTGTA 600  
 40 CTCTTCTCTG ATCGGCCCGC CGCTGCTCAC CCTGGTGAAC TTTGAAGTGG AAAATCTGGC 660  
 GTACATGCTG GTGTGCATGC AGTGGGCGGA TTTGCTCTGG GCCGCCAGCT TCTATGCCCG 720  
 45 CTCTTCTTA TCCTACCTCC CCTTCTACGG CGTCCCTGGG GTGCTGCTCT TCTTTGTGTC 780  
 TGTCAGGGTC CTGGAAAGCC ACTGGTTCGT GTGGATCACA CAGATGAACC ACATCCCCAA 840  
 GGAGATCGGC CACGAGAAGC ACCGGGACTG GGTCACTCT CAGCTGGCAG CCACCTGCAA 900  
 50 CGTGAGGCC TCACTTTTCA CCAACTGGTT CAGCGGGCAC CTCAACTTCC AGATCGAGCA 960  
 CCACCTCTTC CCCAGGATGC CGAGACACAA CTACAGCCGG GTGGCCCCGC TGCTCAAGTC 1020  
 55 GCTGTGTGCC AAGCACGGCC TCAGCTACGA ATGAAGCCCT TCCTCACCCT GCTGGTGGAC 1080  
 ATCGTCAGGT CCCTGAAGAA GTCTGGTGAC ATCTGGCTGG ACGCCTACCT CCATCAGTGA 1140  
 AGGCAACACC CAGGCGGGCA GAGAAGGGCT CAGGGCACCA GCAACCAAGC CAGCCCCCGG 1200  
 60

CGGGATCGAT ACCCCCACCC CTCCACTGGC CAGCCTGGGG GTGCCCTGCC TGCCCTCCTG 1260  
 GTACTGTTGT CTTCCCTCTG GCCCCTCAC ATGTGTATTC AGCAGCCCTA TGGCCTTGGC 1320  
 5 TCTGGGCCTG ATGGGACAGG GGTAGAGGA AGGTGAGCAT AGCACATTTT CCTAGAGCGA 1380  
 GAATTGGGGG AAAGCTGTTA TTTTATATT AAAATACATT CAGATGTAAA AAAAAAAAAA 1440  
 10 AAAAACTCGA GGGGGGGCCC CGGNAACCAA TTCGCCCT 1478

## (2) INFORMATION FOR SEQ ID NO: 64:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2033 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

GGCACGAGGA AGAACGCAAA GCTGAGAACA TGGACGTTAA TATCGCCCCA CTCCGCGCCT 60  
 25 GGGACGATTT CTTCCCGGGT TCCGATCGCT TTGCCCGGCC GGACTTCAGG GACATTTCCA 120  
 AATGGAACAA CCGCGTAGTG AGCAACCTGC TCTATTACCA GACCAACTAC CTGGTGGTGG 180  
 30 CTGCCATGAT GATTTCCATT GTGGGGTTTC TGAGTCCCTT CAACATGATC CTGGGAGGAA 240  
 TCGTGGTGGT GCTGGTGTTC ACAGGGTTTG TGTGGGCAGC CCACAATAAA GACGTCCTTC 300  
 GCCGGATGAA GAAGCGCTAC CCCACGACGT TCGTTATGGT GGTCAATGTT GCGAGCTATT 360  
 35 TCCTTATCTC CATGTTTGA GAGTCATGG TCTTTGTGTT TGGCATTACT TTTCTTTTGC 420  
 TGTGTAGTGT TATCCATGCA TCGTTGAGAC TTCGGAACCT CAAGAACAAA CTGGAGAATA 480  
 40 AAATGGAAGG AATAGGTTTG AAGAGGACAC CGATGGGCAT TGTCTGGAT GCCCTAGAAC 540  
 AGCAGGAAGA AGGCATCAAC AGACTCACTG ACTATATCAG CAAAGTGAAG GAATAAACAT 600  
 AACTTACCTG AGCTAGGGTT GCAGCAGAAA TTGAGTTGCA GCTTGCCCTT GTCCAGACCT 660  
 45 ATGTTCTGCT TGCCTTTTGG AAACAGGAGG TGCACGTACC ACCCAATTAT CTATGGCAGC 720  
 ATGCATGTAT AGGCCGAACT ATTATCAGCT CTGATGTTTC AGAGAGAAGA CCTCAGAAAC 780  
 50 CGAAAGAAAA CCACCACCTT CCTATTGTGT CTGAAGTTTC ACGTGTGTTT ATGAAATCTA 840  
 ATGGGAAATG GATCACACGA TTTCTTTAAG GGAATTAAAA AAAATAAAG AATTACGGCT 900  
 TTTACAGCAA CAATACGATT ATCTTATAGG AAAAAAAAAAT CATGTAAAG TATCAAGACA 960  
 55 ATACGAGTAA ATGAAAAGGC TGTAAAGTA GATGACATCA TGTGTTAGCC TGTTCCTAAT 1020  
 CCCCTAGAAT TGTAATGTGT GGGATATAAA TTAGTTTTTA TTATTCTCTT AAAAATCAAA 1080  
 60 GATGATCTCT ATCACTTTGC CACCTGTTTG ATGTGCAGTG GAAACTGGTT AAGCCAGTTG 1140

5 TTCATACTTC CTTTACAAAT ATAAAGATAG CTGTTTAGGA TATTTTGTTA CATTTTGTGA 1200  
 AATTTTGTGA ATGCTAGTAA TGTGTTTCA CCAGCAAGTA TTTGTTGCAA ACTTAATGTC 1260  
 ATTTTCCTTA AGATGGTTAC AGCTATGTAA CCTGTATTAT TCTGGACGGA CTTATTAAAA 1320  
 TACAAACAGA CAAAAAATAA AACAAAACCT GAGTTCTATT TACCTTGCAC ATTTTGTGTT 1380  
 10 GTTACAGTGA AAAAAATGGT CCAAGAAAAT GTTTGCCATT TTGCAATTGT TTCGTTTTTA 1440  
 ACTGGAACAT TTAGAAAGAA GGAAATGAAT GTGCATTTTA TTAATTCCTT AGGGGCACAA 1500  
 GGAGGACAAT AATAGCTGAT CTTTGAAT TTGAAAAACG TCTTTAGATG ACCAAGCAAA 1560  
 15 AAGCTTTAAA AAATGGTAAT GAAATGGAA TGCAGCTACT GCAGCTAATA AAAAATTTTA 1620  
 GATAGCAATT GTTACAACCA TATGCCTTTA TAGCTAGACA TTAGAATTAT GATAGCATGA 1680  
 20 GTTATACAT TCTATTATT TTCTCCCTT TCTCATGTTT TTATAAATAG GTAATAAAAA 1740  
 ATGTTTGGC TGCCAATTGA ATGATTTTCGT AGCTGAAGTA GAAACATTTA GGTTCCTGTA 1800  
 GCATTAAATT GTGAAGACAA CTGGAGTGGT ACTTACTGAA GAACTCTCT GTATGTCCTA 1860  
 25 GAATAAGAAG CAATGATGTG CTGCTTCTGA TTTTCTTGC ATTTTAAATT CTCAGCCAAC 1920  
 CTACAGCCAT GATCTTAGC ACAGTGATAT CACCATGACT TCACAGACAT GGTCTAGAAT 1980  
 30 CTGTACCCTT ACCCACAAT GAAGAATAAA ATTGATTAAA GGTAAAAAA AAA 2033

35 (2) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 440 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

45 ATGTTTCTTA CTAGAATACT GTGTCCAACC TATATAGCCC TAACTTTCCT GGTITACATT 60  
 GTGGCCCTAG TATCTGGCA GCTGTGCATG GAGATAGCCA GAGGAAACAT TTTTCTTCTT 120  
 AATGAATTGG TGACCACATT TTGTGTTCT TGCCTCCTAT TATCCGTGCC CTATTGTCAT 180  
 50 CCTGGTTTCT TCTACAGTAG TTTATGTAAA TGTGTTTGT TCCTTGTCGT TCTCAGTAGA 240  
 ATTGGTTCTG TAAACGAAAC CTGGTCCTGT AATTTCASTA TATGCTCATA TCTCATCTTT 300  
 55 GGCTCTCCCA TTTTCACAGC ACTGATCCCT AAAAGATGTG CCCTAGAGGA TATCCAGAAC 360  
 AATCCAATTG GATGTCTTCT CCGTGCCT CCAGCCTGGG AGACAGAGGG AGACTCNATC 420  
 TCAAAAAAAA TAAAAAAA 440  
 60



5 (2) INFORMATION FOR SEQ ID NO: 66:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 3301 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
10 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

15	GGTCATAAGG GGAGGGTTGN NGTGTGTCCC TCCAGGTTGT GCAGAGGGGA TTAGAAGTAA	60
	GTAGGTTAGA GGGGAGGTGG AGGGAGTGTG CTGGGTGTG AGCTTTTATG ATGCTGAAAG	120
	GATCATGATA TGCTAAGGAC AGGATAGTGT TGGGTGTGAC ACACAGGTGT AGGCAATCCT	180
20	GGTGGCTAGT ATGTAAAAGT GAATGTCCTG ACTCCCTTAG AGGGTACCTG NCAGAGTGCC	240
	CTTGARGGA CTAGTGCTGG AGAAATTAAT AGGAGAGGGG ACGGGCATCC ATTAACCTTT	300
25	TCTTGCCTGC AGCCTGTAGG GTCCAGCGTC AAAGCGAATC ATGGGGTCCA GGGCTGAGCT	360
	GTGCACTCTC TTAGGCGGAT TCTCCTTCCT CCTGCTACTG ATACCAGGCG AGGGGGCCAA	420
	GGGTGGATCC CTCAGAGAGA GTCAGGGAGT CTGCTCCAAG CAGACACTGG TGGTCCCCTG	480
30	CCACTACAAC GAGTCCTACA GCCAACCAGT GTACAAGCCC TACCTGACCT TGTGCGCTGG	540
	GAGCGCATCT GCAGCACTTA CAGGACCATG TACCGCGTTA TGTGGCGGGA GGTGAGGCGG	600
35	GAGGTTTCAGC AGACCCATGC AGTGTGCTGC CAGGGCTGGA AGAAGCGGCA CCCGGGGGCG	660
	CTCACCTGTG AAGCCATCTG CGCCAAGCCT TGCCTGAACG GAGGCGTCTG CGTTAGGCCT	720
	GACCAGTGCG AGTGCGCCCC CGGCTGGGGA GGAAGCACT GTCATGTGGA CGTGGATGAA	780
40	TGTAGGACCA GCATCACCTT CTGCTCGCAC CATTGTTTAA ATACGGCARG CAGCTTCAMC	840
	TGCGGCTGCC CCATGACCTA GTGCTAGGCG TGGACGGGCG CACCTGCATG GAGGGGTCCC	900
	CAGAGCCCCC AACCAGTGCC AGCATACTCA GCGTGGCCST TCGGGARGCG GAAAAAGATG	960
45	ACGCGCTCTG AAGCAGGAGA TTCACGAGCT GCGAGGCCCT TGAAGCGGCT GGAGCAGTGG	1020
	NCCGGTCAGC TGGGCCCTGG NTCAGACGGT GCTGCCCGTG CCGCCTGAAG WGCTGCAGCC	1080
50	AGAACAGGTG GCTGAGCTGT GGGGCCGGGG TGACCGGATC GAATCTCTCA GCGACCAGGT	1140
	GCTGCTGCTG GAGGAGAGGC TAGGTGCCTG CTCCTGTGAG GACAACAGCC TGGGCCTCGG	1200
55	CGTCAATCAT CGATAAGAAG CCTCTACAGC ACCCCTGCCC CCTAATTTAT ACAGAAACCG	1260
	GACCCACTAA TCCTCTGGGA TTGGCCGACT GTGAGCTGCA GATAAGGCTA TCAGCCACCA	1320
	AAGAGCAATG AACAAATGGAA ACTTCAGAGA GCTGAAGAAA GGGGGAGGCC TGTGTTCTTG	1380
60	GCCTGCCCTT GAGTCTTCTG GCTGGGGGCA GGTTCCTGG GCAAGAACTG CTTCCTCAAT	1440

	TCCTTAACAA ATGCAACCAC CAACACCCAG ATCTCTCTCT CTCPTTATTT TCAGTTTTTT	1500
5	TGCTGTTATC CAGATAATTA ATAAAAACCA ACCACGCAA ACTGGGTCCC ACCCTCTCCT	1560
	TTTGCTCCCA GCCTACCTCC CCAGTTGTGG GAACAGGTCT GGAGTGAGAG GCAGGGAGTG	1620
	GCTAATGCCN CCAGGAAGAA ATGAAAACCTG GCTCAGAGAG GGGGAAGCCT CAACAGAAAA	1680
10	AGAAATAAAT TAAAAGCCCT CCTATCCCCT CCAGCCAGGG TTCGTTCCCTT TCCCCAACTC	1740
	CCCAGGGGGC AGAAGTGAGT GCAGCACCTG ATGTCTGCTT CTTCCCCTTG TGTCTGGTGA	1800
15	GATGGTGAGC CAGGGCTGCA GGGGGCTGGG TGGGGTCATG TCCACTGAAG AACTGTACTA	1860
	TGGGGACAGA AAACCAGAAA TGTGGAGACT GAACTGGTAT CCCAGAGAGT GCACGACCCT	1920
	GGGCATCTGG GCAAGGGCAG GCATGAGACC TCTGAATTAG AAGGTCCAG CCCCCACTGA	1980
20	CAGGAGGCTA CACTGGGAGG GAAGGTGAAG GTGCTGAGGA AAGCTCCCAT GATGAGCCTG	2040
	GGAGTGCTTC AGGTATCAGC TTCCAGCCAG AGGGCGAGAA GTCCTCCTCA CAAATGGATG	2100
25	AGTCCATTGA ATCCATGGAC TTTGGAGTGG GGGGGATTG TTCCAAAGAA TGGATGAGTC	2160
	CACTGGCCAA TGTGGGGTAG AGGGGTAGAG AAGACCACAT AGGAAGAGAC TCCACTGGGG	2220
	ATGGAATGTT CCCCTCCCTT GTGTAGGCTG AGTCACTGGA GATGAGGGGG AGGCAACTGT	2280
30	CCCACAGACA ARACAGTAGG AGGTGGGGGT CAAGAGTGA GACTGCACCG AGGCAAGAGT	2340
	CCATGGATGG GGCCAAGAGG GGGCAGGAGT GGCCTGTAT CCACATTTCA CTTCAGAAGT	2400
35	TGAAGATTCC AAAGAGGAGA ATAAGTGGGG AGAGGGGAGA CAAGGAAGAG GGTTTTGCCC	2460
	TGCTTCAGGG CCCACTGGGT GGGTAGGTGT GGGGAGGAAG ATGGGGACAG ATGGGAGGAG	2520
	AGCTCAGAGC CAGGGTTTAC CCACCGCCCC CAGGCTTCTT CAGATAGTCA CCACCACCCC	2580
40	GGCCATCAGT GGAGATTTC CGGAAAACAG TGAAGCATGG AGTGCCGAC TCTGTGAGCC	2640
	AGAGCTGGGA CGTCATCTGG TGTGAGCCCT TCCGTGGGCA CTGGGGGCAG CACCCGCACC	2700
45	TGACATTGTC CCGAGGTGAA GCGACGCTCC TTCTTGCACT AGAAGTCTTG GTAGGAGGAC	2760
	ATGACTATGG GGACAATGGG AACCTGGGCC TGCCTGCAA GATGGAAGGC GCCACGTTTG	2820
	AAGGGCAGCA TGGAGCCATT GTGGTTTCTC GTTCCTCAG GAAACACCCA GACCTTCACG	2880
50	TCCTGGGTGA GCAGGGTCTG GCGACCTCA GACATGACAC TGATGGCATC CCCCCTGCGC	2940
	TTCCGGTCGA TGAAGATGAC TCCTGCCAGC CAGCAGGCCA GCCCGCAGAG CCAGCCCACA	3000
55	GTANTCGCGC TTGGCAATGG GCACACAGCG GCCTGGCAGT ACCTCCATCA TCCCAAGCAG	3060
	ATCGAGAGAG CTCTGGTGGT TGGAGACAAC AACATAGGGC TCGAGGGAG GGAAGTGGTG	3120
	AGCCCCTCGC ACCTCCACTC GGATCCCGTA CAGGTATTTG ATGTGGAGCA GCATTAGACG	3180
60	CAAGATCTTC ATGTTCTCGA CGTTGCGTCC TCGCACGGCA CACACAGGGA TGGCGAGCAC	3240

AGCCAGGAAG AGGATCCAGC CATGTAGAA GGCCATCTTG AAGAAGTACT TGGCACTGGG 3300  
5 G 3301

10 (2) INFORMATION FOR SEQ ID NO: 67:

(i) SEQUENCE CHARACTERISTICS:  
15 (A) LENGTH: 1535 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

20 GGCACGAGGT CAAGCGAAAG GATTTCAGG AACAGATCAT CCACCATGTG TTCACCATCA 60  
TTCTCATCAG CTTTTCCTGG TTTGCCAATT ACATCCGAGC TGGGACTCTA ATCATGGCTC 120  
TGCATGGACT CTTCGGATTA CCTGCTGGAG TCAGCCAAGA TGTTTAACTA CGCGGGATGG 180  
25 AAGAACACCT GCAACAACAT CTTTCATCGTC TTCGCCATTG TTTTATCAT CACCCGACTG 240  
GTCATCCTGC CCTTCTGGAT CCTGCATTGC ACCCTGGTGT ACCCACTGGA GCTCTATCCT 300  
GCCTTCTTTG GCTATTACTT CTTCAATTCC ATGATGGGAG TTCTACAGCT GCTGCATATC 360  
30 TTCTGGGCCT ACCTCATTTT GCGCATGGCC CACAAGTTCA TAACTGGAAA GCTGGTAGAA 420  
GATGAACGCA GTACCGGGAA GAAACAGAGA GCTCAGAGGG GGAGGAGGCT GCAGCTGGGG 480  
35 GAGGAGCAAA GAGCCGGCCC CTAGCCAATG GCCACCCCAT CCTCAATAAC AACCATCGTA 540  
AGAATGACTG AACCATTATT CCAGCTGCCT CCCAGATTAA TGCATAAAGC CAAGGAACTA 600  
CCCCGCTCCC TGCCTATAG GGTCACCTTA AGCTCTGGGG AAAAAGGAGA AAGTGAGAGG 660  
40 AGAGTTCTCT GCATCCTCCC TCCTTGCTTG TCACCCAGTT GCCTTTAAAC CAAATTCTAA 720  
CCAGCCTATC CCCAGGTAGG GGGACGTTGG TTATATTCTG TTAGAGGGGG ACGGTCGTAT 780  
45 TTCTCTCCCT ACCCGCCAAG TCATCCTTTC TACTGCTTTT GAGGCCCTCC CTCAGCTCTC 840  
TGTGGGTAGG GGTTACAATT CACATTCCTT ATTCTGAGAA TTTGGCCCA GCTGTTTGCC 900  
TTTGACTCCC TGACCTCCAG AGCCAGGGTT GTGCCTTATT GTCCCATCTG TGGGCCTCAT 960  
50 TCTGCCAAAG CTGGACCAAG GCTAACCTTT CTAAGCTCCC TAACTTGGGC CAGAAACCAA 1020  
AGCTGAGCTT TTAACCTTCT CCCTCTATGA CACAAATGAA TTGAGGGTAG GAGGAGGGTG 1080  
55 CACATAACCC TTACCCTACC TCTGCCAAAA AGTGGGGGCT GTACTGGGGA CTGCTCGGAT 1140  
GATCTTCTTT AGTGCTACTT CTTTCAGCTG TCCCTGTAGC GACAGGTCTA AGATCTGACT 1200  
GCCTCCTCCT TTCTCTGGCC TCTTCCCCCT TCCCTCTTCT CTTTCAGCTAG GCTAGCTGGT 1260  
60

TTGGAGTAGA ATGGCAACTA ATTCTAATTT TTATTATTATTA AATATTTGGG GTTTTGGTTT 1320  
 TAAAGCCAGA ATTACGGCTA GCACCTAGCA TTTCAGCAGA GGGACCATTT TAGACCAAAA 1380  
 5 TGTACTGTTA ATGGGTTTTT TTTTAAAATT AAAAGATTAA ATAAAAAATA TTAAATAAAA 1440  
 CATGGCAATA AGTGTACAGAC TATTAGGAAT TGAGAAGGGG GATCAACTAA ATAAACGAAG 1500  
 10 AGAGTCTTTC TTATGCAAAA AAAAAAAAAA AAAAA 1535

15 (2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1244 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 20 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

25 GGGCACCCAC CAGCGGCGCC GACCTCAGCG CGCACCTATG GGCTCGCTAC CAGGACATGC 60  
 GGAGACTGGT GCACGACCTC CTGCCCCCGG AGGTCTGCAG TCTCCTGAAC CCAGCAGCCA 120  
 TCTACGCCAA CAACGAGATC AGCCTGCGTG ACGTTGAGGT CTACGGCTTT GACTACGACT 180  
 30 ACACCCCTGGC CCAGTATGCA GACGCACTGC ACCCCGAGAT CTTCACTACC GCCCGTGACA 240  
 TCCTGATCGA GCACTACAAG TACCCAGAAG GGATTCGGAA GTATGACTAC AACCCAGCT 300  
 35 TTGCCATCCG TGGCTCCAC TATGACATTC AGAAGAGCCT TCTGATGAAG ATTGACGCCT 360  
 TCCACTACGT GCAGCTGGGG ACAGCCTACA GGGGCTCCA GCCTGTGCCA GACGAGGAGG 420  
 TGATTGAGCT GTATGGGGGT ACCCAGCACA TCCCACTATA CCAGATGAGT GGCTTCTATG 480  
 40 GCAAGGGTCC CTCCATTAA GAGTTTCATG ACATCTTCTC GCTACCGGAG ATGGCTCTGC 540  
 TGTCTGTGT GGTGGACTAC TTTCTGGGCC ACAGCCTGGA GTTTGACCAA GCACATCTCT 600  
 ACAAGGACGT GACGGACGCC ATCCGAGACG TGCATGTGAA GGGCCTCATG TACCAGTGGA 660  
 45 TCGAGCAGGA CATGGAGAAG TACATCCTGA GAGGGATGA GACGTTTGCT GTCCTGAGCC 720  
 GCCTGGTGGC CCATGGGAAA CAGCTGTTCC TCATCACCAA CAGTCCTTTC AGCTTCGTAG 780  
 50 ACAAGGGGAT GCGGCACATG GTGGGTCCCG ATTGGCGCCA CTCTTCGATG TGGTCATTGT 840  
 CCAGGCAGAC AAGCCAGCT TCTTCACTGA CCGGCGCAAG CTTTNCAGAA AACTCGATGA 900  
 GAAGGGCTCA CTTCACTGGG ACCGGATCAC CCGCTTGGA AAGGCAAGA TCTATCGGCA 960  
 55 GGGAAACCTG TTTGACTTCT TACGCTTGAC GGAATGGCGT GGCCCCGCG TGCTCTACTT 1020  
 CGGGGACCAC CTCTATAGTG ATCTGGCGGA TCTCATGCTG CGGCACGGCT GGCGCACAGG 1080  
 60 CGCCATCATC CCCGAGCTGG AGCGTGAGAT CCGCATCATC AACACGGAGC AGTACATGCA 1140

CTCGCTKACG TGGCAGCAGG CGCTCACGGG GCTKCTKGAG CGCATKCAGA CCTATCAGGA 1200  
 CGCGGAGTTG AGGCAGGTCT TGCTTCCTTG ATGAAAGANC GNNT 1244  
 5

(2) INFORMATION FOR SEQ ID NO: 69:  
 10

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1292 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

GGCAGGAGCA GCGACGCGAC TCTGGTGGCG GCCGTCTTCT TCCCCCGAG CTGGGCGTGC 60  
 20 GCGGCCGCAA TGAAGTGGGA GCTGCTGCTG TGGCTGCTGG TGCTGTGCGC GCTGCTCCTG 120  
 CTCCTGGTGC AGCTGTGCGG CTTCTGAGG GCTGACGGCG ACCTGACGCT ACTATGGGCC 180  
 25 GAGTGGCAGG GACGACGCCC AGAATGGGAG CTGACTGATA TGGTGGTGTG GGTGACTGGA 240  
 GCCTCGAGTG GAATTGGTGA GGAGCTGGCT TACCAGTTGT CTAAACTAGG AGTTTCTCTT 300  
 GTGCTGTCTAG CCAGAAGAGT GCATGAGCTG GAAAGGGTGA AAAGAAGATG CCTAGAGAAT 360  
 30 GGCAATTTAA AAGAAAAAGA TATACTTGTT TTGCCCCTTG ACCTGACCGA CACTGGTTCC 420  
 CATGAAGCGG CTACCAAAGC TGTCTCCAG GAGTTTGTA GAATCGACAT TCTGGTCAAC 480  
 35 AATGGTGGAA TGTCCAGCG TTCTCTGTGC ATGGATACCA GCTTGGATGT CTACAGAAAG 540  
 CTAATAGAGC TTAAGTACTT AGGGACGGTG TCCTTGACAA AATGTGTTCT GCCTCACATG 600  
 ATCGAGAGGA AGCAAGGAAA GATTGTTACT GTGAATAGCA TCCTGGGTAT CATATCTGTA 660  
 40 CCTCTTTCCA TTGGATACTG TGCTAGCAAG CATGCTCTCC GGGGTTTTTT TAATGGCCTT 720  
 CGAACAGAAC TTGCCACATA CCCAGGTATA ATAGTTTCTA ACATTTGCCC AGGACCTGTG 780  
 45 CAATCAAATA TTGTGGAGAA TTCCCTAGCT GGAGAAGTCA CAAAGACTAT AGGCAATAAT 840  
 GGAGACCACT CCCACAAGAT GACAACCACT CGTTGTGTGC GGCTGATGTT AATCAGCATG 900  
 GCCAATGATT TGAAAGAAGT TTGGATCTCA GAACAACCTT TCTTGTTTAG TAACATATTT 960  
 50 GTGGCAATAC ATGCCAACCT GGGCCTGGTG GATAACCAAC AAGATGGGGA AGAAAAGGAT 1020  
 TGAGAACTTT AAGAGTGGTG TGGATGCAGA CTCTCTCTAT TTTAAATCT TTAAGACAAA 1080  
 55 ACATGACTGA AAAGAGCAAC TGTACTTTTC AAGCCACTGG AGGGAGAAAT GGAAAACATG 1140  
 AAAACAGCAA TCTCTTATG CTTCTGAATA ATCAAAGACT AATTTGTGAT TTTACTTTTT 1200  
 AATAGATATG ACTTTGCTTC CAACATGGAA TGAAATAAAA AATAAATAAT AAAAGATTGC 1260  
 60

CATGAATCTT GCAAAAAAAAA AAAAAAAAA AA

1292

5

(2) INFORMATION FOR SEQ ID NO: 70:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 1031 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

15

GGGCTGTTGC TTTTGAACAG AACCTATAT TACTCTCCTG GGATCTGAGT TTCTGCAGGT 60

CATTTGTATG TAGGACCAGG AGTATCTCCT CAGGTGACCA GTTTTGGGGA CCCGTATGTG 120

20

GCAAAITCTA AGCTGCCATA TTGAACATCA TCCCACTGGG AGTGGTTATG TTGTATCCCC 180

ATCTTGGCTG GCTTCAGTTT TTGCTGTAGC CCTAGAGCAC TTGTTTTGTG GGAGGCTGGC 240

CTCTTGCCTA CTCCTTGCA TGGACAGGGG GATGAATATT TACTTTCCA CCTCCTTGCT 300

25

TTTTCTTTCA CTGATACCAC TGAATGGAAC TGGTGCTGTG ACTCCTGCTG CTGGGGATTT 360

ATGTCCCAG ACCTTAGCCT GGCTGAGTGG AGCCTGAGAC CTGCACAACA GCTCATGGTC 420

30

ATGCATGARA GAGAAGTGGC TGGCCACAGC AGAGGGAACA GTAACAGCCC AGGGGCCTTT 480

ATTTTGGGAA AGGCTGTCCG GGGCTGTTAC TGTCTCTTCT GGTATAAAG CAGACATGTG 540

GCCATCTTTT CCGCAGGTTA GAGTGGGCTC CTTTCTTTTT GGAATCCTTT TCTTCTCCTT 600

35

TGGTAGCAGC TCCCTGCCTC CAGGGCTTCC GCCACCAGCG TCTCTGCTGT GTTGCGCAGT 660

GCAGTGGGGT GCAAGGGCTT TGTTCCTGCC TGCCTGAAAG AGAGGGCTCT GGGGATGGAG 720

40

ATGAGAAACA ACACGCTCTC CTTCAGACAA TGAGGCATTG TGTCTCTCTG CTGCCATTCT 780

TCATCTCCAC TGAGAGCCAG AGCTGGTAGG AGCCGAGTGC CACAGGCATT CTGCATTGCT 840

CTACTCTTAG GTTTGTGTGT GTGATCCTTC CCCTCCCTGT CGCCCACTCC TCCCTCCTCT 900

45

GGCTATCCTA CCCTGTCTGT GGGCTCTTTT ACTACCAGCC TATGCTGTGG GACTGTGATG 960

GCATTTAGTT CAGAGTGGAN GGGCTTTGGS CTGAAATAAA ATGCAAGTAT TTAACAAAAA 1020

50

AAAAAAAAA A 1031

-55

(2) INFORMATION FOR SEQ ID NO: 71:

(i) SEQUENCE CHARACTERISTICS:

60

(A) LENGTH: 855 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

5 AGCTATTGAC ACTTCCTGGT GGGATCCGAG TGAGGCGACG GGGTAGGGGT TGGCGCTCAG 60  
 GCGGCGACCA TGGCGTATCA CGGCCTCACT GTGCCTCTCA TTGTGATGAG CGTGTTCTGG 120  
 GGCTTCGTCG GCTTCTTGGT GCCTTGGTTC ATCCCTAAGG GTCCTAACCG GGGAGTTATC 180  
 10 ATTACCATGT TGGTGACCTG TTCAGTTTGC TGCTATCTCT TTTGGCTGAT TGCAATTCTG 240  
 GCCCAACTCA ACCCTCTCTT TGGACCGCAA TTGAAAAATG AAACCATCTG GTATCTGAAG 300  
 15 TATCATTGGC CTTGAGGAAG AAGACATGCT CTACAGTGCT CAGTCTTTGA GGTCACGAGA 360  
 AGAGAATGCC TTCTAGATGC AAAATCACCT CCAAACCAGA CCACTTTTCT TGA CTGTCCT 420  
 GTTTTGGCCA TTAGCTGCCT TAAACGTAA CAGCACATTT GAATGCCTTA TTCTACAATG 480  
 20 CAGCGTGTTT TCCTTTGCCT TTTTGCCT TGGTGAATT ACGTGCCTCC ATAACCTGAA 540  
 CTGTGCCGAC TCCACAAAAC GATTATGTAC TCTTCTGAGA TAGAAGATGC TGTCTTCTG 600  
 25 AGAGATACGT TACTCTCTCC TTGGAATCTG TGGATTTGAA GATGGCTCCT GCCTTCTCAC 660  
 GTGGAATCA GTGAAGTGT TAGAACTGC TGCAAGACAA ACAAGACTCC AGTGGGGTGG 720  
 TCAGTAGGAG AGCACGTTCA GAGGGAAGAG CCATCTCAAC AGAATCGCAC CAACTATAC 780  
 30 TTTCAGGATG AATTCTTCT TCTGCCATC TTTTGAATA AATATTTTCC TCCTTTCTAW 840  
 RRAAAAAAAA ANANN 855

35

(2) INFORMATION FOR SEQ ID NO: 72:

40 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1274 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

GGCAGAGCTT AGAGTGTGGA AAAGGCAACC AGGTTGGCCG TAAGTGCCCTG CTGGAATGCG 60  
 50 TGTGCCTCCA CACGGTCTG GGCATCCGA CTGATAACCA GCCGGCCAGA CTGAGGGATG 120  
 GAAGGCACTG AGATGGGGC CCGTCCAGGC GGACACCCGC AGAAATGGAG CTTTCTGTGG 180  
 TCTCTGCAC TCTGGCTGCC TCTTGCCCTC TCTGTGCTC TCTTCTTGG TCTCTCCCTC 240  
 55 TCTCTCCTC AGCCTGGTCT TCTCTTTGG TGCACACTTA GTTATTGTTG TGAGCAATGG 300  
 AAGTCAAAG GAACTCCCTC TCCAGCTCTT CTGAATCTTG GGACACAGCC TAAAAAGGAC 360  
 60 AAAAAGTTAG AAGACAGCAT AGCAACTCAG CTCAGGGAGC TACCAGAGAA AAATAGCAAC 420

5 TGATGTGGGT GCTTTTTTTT TTTTTTTAAT TTGAATAAAA AGAATTAGAA GTGATGTCCT 480  
 TTTATAAAAT GCCTTCTCCC CCTTCCCGCC TACAGTCTCT TCCTCTCCCC TTAGAGGGGG 540  
 GAAAGTGTAT AAACCTACAG GGTGTGTAGT CTGAAAAGAG GATCCCCCTC ACCCCCACCC 600  
 TGGGCAGAGC AGTGGGGGTT GGGGGGTGGG AGAGGGGGAC ACAGATCCTG GCACACTGTG 660  
 10 GATATTTCTT GCAGATTGCA GTCTCTGTG GCCCAAACAG GTTAGGTAGA CTATCGCCTC 720  
 TGGCAGGTGC CACCTTTTGG TACCAACATG TTCTGAGGTG TTAGGATTG GGTGGGTTT 780  
 TTTTGTTTG TTTTTTTTTT CCTTTTGGTC TTTTTTTTTT TCTCCTTTTA AAGAAAAGCT 840  
 15 AAAGCCGCT GTGAGTCTG GTGGCAGGCT CTCCATGGAT GTAGCATATC GAAGATAATT 900  
 TTTATACTGC ATTTTATG ATTTATTTGT AATGTGTGAT TCCGTCTGCT GAGGAGGTG 960  
 20 GAGGGGCTCC AGGGAAAGCC ACCCACCTTC AGTGAGGTG CTCCCCAGCT GAGCGCACCG 1020  
 GGCATGGGAT GTGGAGGCTG GCGACACACC CTGTGCCTCT CCAAGGCTGG GCGCGTGGGG 1080  
 CGTCCAGAGT CTCTCTGGGT CTCAGATGTC CATCTGCCAC CTCTTGTTAA GGCTCTAGCC 1140  
 25 AGAAGGGAGG GTGAGGGTAG AAGAAAGTTA TTCCCGAAGA AAAAAAGAAAT GAAAAGTCAT 1200  
 TGTACTGAAC TGTTTTTATA TTTTAAAAAG TTACTATTWA AAGGTAAAAA AAAGGGGGGG 1260  
 30 CCCGGTACCC AATT 1274

35 (2) INFORMATION FOR SEQ ID NO: 73:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 688 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

45 GGCACGAGTG GAGGCAATGC CAGCTCCAGG ACAGAGGCTC AGGTGCCCAA CGGGCAAGGC 60  
 AGCCAGGGG GCTGTGTCTG TTCAAGTCAG GCTTCCCCGG CCTCGCGCA CAGCGCTTCC 120  
 ACGGCAGCC CGGGGCCCCA CCCCACGCAC TGAAGAGGCC GCCTGGGCTG CCATGGCCCT 180  
 50 GACCTTCCTG CTGGTGCTGC TCACCTGGC CACGTCTGCA CACGGCTGCA CAGAACTTC 240  
 CCACGCGGG AGAGCATCTA CTGGGGGCC ACAGCGGACA GCCAGGACAC AGTGGCTGCT 300  
 55 GTGCTGAAGC GGAGGCTGCT GCAGCCCTCG CGCCGGGTCA AGCGCTCGCG CCGGAGACCC 360  
 CTCTCCCGCC CACGCCGGAC AGCGGCCCGG AAGCGAGAG CTCGGAGTGA CGGCCTGGGA 420  
 60 CCTGCCACTG TGGCGTGGG CTCTCCCCG CGCCGCGAGG CCGCGACCTC TGCCACGTGG 480



ACCGCGCGCG GGGCGCTCCC TGGTGGCGAT GGCGCGGCAC TGGCCGAGCA CTGCGGGGGC 540  
 TTCTCTCCTT GTTGGTTGCT GAGTGGGCGG CCAAGGGGAG AAAAGGAGCC GCTTCTGCCT 600  
 5 CCCTTGCCAA AACTCCGTTT CTAATTAAAT TATTTTGTAGT AGAAAAAAAA AAAAAAAAAA 660  
 AAAAAAAAAA AAAAAAAAAA AAAAAA 688

10

(2) INFORMATION FOR SEQ ID NO: 74:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1890 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

GAGCAGGAGA GAAGGCACCG CCCACCCCCG CCTCCAAAGC TAACCCTCGG GCTTGAGGGG 60  
 AAGAGGCTGA CTGTACGTTT CTTCTACTCT GGCACCACTC TCCAGGCTGC CATGGGGCCC 120  
 25 AGCACCCCTC TCCTCATCTT GTTCCTTTTG TCATGGTCGG GACCCCTCCA AGGACAGCAG 180  
 CACCACCTTG TGGAGTACAT GGAACGCCGA CTAGCTGCTT TAGAGGAACG GCTGGCCAG 240  
 30 TGCCAGGACC AGAGTAGTCG GCATGCTGCT GAGCTGCGGG ACTTCAAGAA CAAGATGCTG 300  
 CCACTGCTGG AGGTGGCAGA GAAGGAGCGG GAGGCACTCA GAACTGAGGC CGACACCATC 360  
 TCCGGGAGAG TGGATCGTCT GGAGCGGGAG GTAGACTATC TGGAGACCCA GAACCCAGCT 420  
 35 CTGCCCTGTG TAGAGTTTGA TGAGAAGGTG ACTGGAGGCC CTGGGACCAA AGGCAAGGGA 480  
 AGAAGGAATG AGAAGTACGA TATGGTGACA GACTGTGGCT ACACAATCTC TCAAGTGAGA 540  
 40 TCAATGAAGA TTCTGAAGCG ATTGGTGGC CCAGCTGGTC TATGGACCAA GGATCCACTG 600  
 GGGCAAACAG AGAAGATCTA CGTGTTAGAT GGGACACAGA ATGACACAGC CTTTGTCTTC 660  
 CCAAGGCTGC GTGACTTCAC CCTTGCCATG GCTGCCCAGA AAGCTTCCCG AGTCCGGGTG 720  
 45 CCCTTCCCCT GGGTAGGCAC AGGCAGCTG GTATATGGTG GCTTCTTTTA TTTGCTCGG 780  
 AGGCCTCTG GAAGACCTGG TGGAGGTGGT GAGATGGAGA AACTTTGCA GCTAATCAAA 840  
 50 TTCCACCTGG CAAACCGAAC AGTGGTGGAC AGCTCAGTAT TCCCAGCAGA GGGGCTGATC 900  
 CCCCCCTACG GCTTGACAGC AGACACCTAC ATCGACCTGG CAGCTGATGA GGAAGGTCTT 960  
 TGGGCTGTCT ATGCCACCCG GGAGGATGAC AGGCACTTGT GTCTGGCCAA GTTAGATCCA 1020  
 55 CAGACACTGG ACACAGAGCA GCAGTGGGAC ACACCATGTC CCAGAGAGAA TGCTGAGGCT 1080  
 GCCTTTGTCA TCTGTGGGAC CCTCTATGTC GTCTATAACA CCCGTCCTGC CAGTCGGGCC 1140  
 60 CGCATCCAGT GTCCTTTGA TGCCAGCGGA CCCTGACCCC TGAACGGGCA GCACTCCCTT 1200

220

5 ATTTTCCCCG CAGATATGGT GCCCATGCCA GCCTCCGCTA TAACCCCGA GAACGCCAGC 1260  
 TCTATGCCTG GGATGATGGC TACCAGATTG TCTATAAGCT GGAGATGAGG AAGAAAGAGG 1320  
 AGGAGGTTTG AGGAGCTAGC CTTGTTTTTT GCATCTTTCT CACTCCCAT AATTTATATT 1380  
 ATATCCCCAC TAAATTTCTT GTTCCTCATT CTTCAAATGT GGGCCAGTTG TGGCTCAAAT 1440  
 10 CCTCTATATT TTTAGCCAAT GGCAATCAAA TTCTTTCAGC TCCTTTGTTT CATACGGAAC 1500  
 TCCAGATCCT GAGTAATCCT TTTAGAGCCC GAAGAGTCAA AACCTCAAT GTTCCCTCCT 1560  
 GCTCTCCTGC CCCATGTCAA CAAATTTTCAG GCTAAGGATG CCCAGAGCCC AGGGCTCTAA 1620  
 15 CCTTGTATGC GGGCAGGCCC AGGGAGCAGG CAGCAGTGTT CTTCCCTCA GAGTGAAGTTG 1680  
 GGGAGGGAGA AATAGGAGGA GACGTCCAGC TCTGTCTCT CTTCTCACT CTTCCCTTCA 1740  
 20 GTGTCTGAG GAACAGGACT TTCTCCACAT TGTTTGTAT TGCAACATTT TGCATTAAAA 1800  
 GGAAATCCA CTGCAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAACGG CACGAGGGGG 1860  
 25 GGTCCCGTAC CCAATNGCCC TCACATGCAT 1890

30 (2) INFORMATION FOR SEQ ID NO: 75:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1133 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 35 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

40 GCCGGTCTGA GTGCAGAGCT GCTGTCATGG CGGCCGCTCT GTGGGGCTTC TTTCCCGTCC 60  
 TGCTGCTGCT GCTGCTATCG GGGGATGTCC AGAGCTCGGA GGTGCCCGGG GCTGCTGCTG 120  
 AGGGATCGGG AGGGAGTGGG GTCGGCATAG GAGATCGCTT CAAGATTGAG GGGCGTGCAG 180  
 45 TTGTTCCAGG GGTGAAGCCT CAGGACTGGA TCTCGCGGC CCGAGTCTG GTAGACGGAG 240  
 AAGAGCACGT CGGTTTCCTT AAGACAGATG GGAGTTTGT GGTTCATGAT ATACCTTCTG 300  
 GATCTTATGT AGTGAAGTT GTATCTCCAG CTTACAGATT TGATCCCGTT CGAGTGGATA 360  
 50 TCACTTCGAA AGGAAAAATG AGAGCAAGAT ATGTGAATTA CATCAAACA TCAGAGGTTG 420  
 TCAGACTGCC CTATCTCTC CAAATGAAAT CTTCAAGTCC ACCTTCTTAC TTTATTAAAA 480  
 55 GGAATCGTG GGGTGGACA GACTTCTTAA TGAACCAAT GGTATGATG ATGGTTCTTC 540  
 CTTTATTGAT ATTTGTGCTT CTGCCTAAAG TGGTCAACAC AAGTGATCCT GACATGAGAC 600  
 60 GGGAAATGGA GCAATCAATG AATATGCTGA ATTCCAACCA TGAGTGCCT GATGTTCTG 660

221

AGTTCATGAC AAGACTCTTC TCTTCAAAT CATCTGGCAA ATCTAGCAGC GGCAGCAGTA 720  
AAACAGGCAA AAGTGGGGCT GGCAAAAGGA GGTAGTCAGG CCGTCCAGAG CTGGCATTGT 780  
5 CACAAACACG GCAACACTGG GTGGCATCCA AGTCTTGAA AACCGTGTGA AGCAACTACT 840  
ATAAACTTGA GTCATCCCGA CGTTGATCTC TTACAACTGT GTATGTTAAC TTTTGTAGCAG 900  
ATGTTTGTGA CTTGGTACAC GAGAAAACCC AGCTTTCATC TTTTGTCTGT ATGAGGTCAA 960  
10 TATTGATGTC ACTGAATTAA TTACAGTGTC CTATAGAAAA TGCCATTAAT AAATTATATG 1020  
AACTACTATA CATTATGTAT ATTAATTAAA ACATCTTAAT CCAGAAAAAA AAAAAAARAA 1080  
15 AACTCGAGGG GGGGCCCGGT ACCCAATTIN CCAAATGGGA GTCGTAAAAA ATC 1133

20 (2) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 585 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

30 ATGTTTACAA TGTGTGTAT AAATGGGACA ACTCCTCGCC CTCTACCTGT CCCCTCCCCC 60  
TTTGGTGTGA TGATTTTCTT CTTTTTAAG AACCCCTGGA AGCAGCGCCT CCTTCAGGGT 120  
TGGCTGGGAG CTCGGCCCAT CCACCTCTTG GGTACCTGC CTCTCTCTCT CCTGTGGTGT 180  
35 CCCCTCCCTC TCCCATGTGC TCGGTGTTCA GTGGTGATA TTTCTTCTCC CAGACATGGG 240  
GCACACGCCC CAAGGGACAT GATCCTCTCC TTAGTCTTAG CTCATGGGGC TCTTTATAAG 300  
40 GAGTTGGGGG GTAGAGGCAG GAAATGGGAA CCGAGCTGAA GCAGAGGCTG AGTTAGGGGG 360  
CTAGAGGACA GTGCTCCTGG CCACCCAGCC TCTGCTGAGA ACCATTCTTG GGATTAGAGC 420  
TGCCCTTCCC AGGGA AAAAG TGTGCTCTCC CCGACCTCC CGTGGGCCCT GTGGTGTGAT 480  
45 GCTGTGTCTG TATATTCTAT ACAAAGGTAC TTGTCCTTC CCTTTGTAAA CTACATTGA 540  
CATGGATTAA ACCAGTATAA ACAGTTAAAA AAAAAAAAAA AAAAA 585

50

(2) INFORMATION FOR SEQ ID NO: 77:

55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 577 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
60 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

5 GGCACGAGGC CTTGCAGAAC TTCTACTTGC CTGCCTCCCT GCCTCTGGCC ATGGCCTGCC 60  
 GGTGCCTCAG CTTCTTCTG ATGGGGACCT TCCTGTCACT TCCCCAGACA GTCCTGGCCC 120  
 AGCTGGATGC ACTGCTGGTC TCCCCAGGCC AAGTGGCTCA ACTCTCCTGC ACGCTCAGCC 180  
 10 CCCAGCACGT CACCATCAGG GACTACGGTG TGTCTGGTA CCAGCAGCG GCAGGCAGTG 240  
 CCCCTCGATA TCTCTCTAC TACCGCTCGG AGGAGGATCA CCACCGGCCT GCTGACATCC 300  
 CCGATCGATT CTCGGCAGCC AAGGATGAGG CCCACAATGC CTGTGTCCTC ACCATTAGTC 360  
 15 CCGTGCAGCC TGAAGACGAC GCGGATTACT ACTGCTCTGT TGGCTACGGC TTTAGTCCCT 420  
 AGGGGTGGGG TGTGAGATGG GTGCCTCCCC TCTGCCTCCC ATTTCTGCCC CTGACCTTGG 480  
 20 GTCCCTTTTA AACTTTCTCT GAGCCTTGCT TCCCCTCTGT AAAATGGGTT AATAATATTC 540  
 AACATGTCAA CAACAAAAA NAAAAWAAA AACTCGA 577

25

## (2) INFORMATION FOR SEQ ID NO: 78:

## (i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 2278 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

35 GTAATCGGC ACGAGGCGCC CAACATGGCG GGTGGGCGCT GCGGCCCGCA SCTAACGGCG 60  
 CTCCTGGCCG CCTGGATCGC GGCTGTGGCG GCGACGGCAG GCCCGAGGA GGCCGCGCTG 120  
 40 CCGCCGAGC AGAGCCGGGT CCAGCCCATG ACCGCCTCCA ACTGGACGCT GGTGATGGAG 180  
 GCGAGTGGA TGCTGAAATT TTACGCCCCA TGGTGTCCAT CCTGCCAGCA GACTGATTCA 240  
 45 GAATGGGAGG CTTTTCGAAA GAATGGTGAA ATACTTCAGA TCAGTGTGGG GAAGGTAGAT 300  
 GTCATTCAAG AACCAGTTT GAGTGGCCGC TTCTTTGTCA CCACTCTCCC AGCATTTTTT 360  
 CATGCAAAGG ATGGGATATT CCGCCGTAT CGTGGCCCAG GAATCTTCGA AGACCTGCAG 420  
 50 AATTATATCT TAGAGAAGAA ATGGCAATCA GTCGAGCCTC TGAATGGCTG GAAATCCCCG 480  
 GCTTCTCTAA CGATGTCTGG AATGGCTGGT CTTTTAGCA TCTCTGGCAA GATATGGCAT 540  
 55 CTTCACTACT ATTTACAGT GACTCTTGA ATCTCTGCTT GGTGTCTTTA TGTCTTTTTC 600  
 GTCATAGCCA CTTGGTTTTT TGGCCTTTTT ATGGGTCTGG TCTTGGTGGT AATATCAGAA 660  
 TGTCTCTATG TGCCACTTCC AAGGCATTTA TCTGAGCGTT CTGAGCAGAA TCGGAGATCA 720  
 60 GAGGAGGCTC ATAGAGCTGA ACAGTTGCAG GATGCGGAGG AGGAAAAAGA TGATTCAAAT 780

GAAGAAGAAA ACAAAGACAG CCTTGTAGAT GATGAAGAAG AGAAAGAAGA TCTTGGCGAT 840  
GAGGATGAAG CAGAGGAAGA AGAGGAGGAG GACAACTTGG CTGCTGGTGT GGATGAGGAG 900  
5 AGAAGTGAGG CCAATGATCA GGGGCCCCCA GGAGAGGACG GTGTGACCCG GGAGGNAAGT 960  
AGAGCCTGAG GAGGCTGAAG AAGGCATCTC TGAGCAACCC TGCCCAGCTG ACACAGAGGT 1020  
10 GGTGGAAGAC TCCTTGAGGC AGCGTAAAAG TCAGCATGCT GNCAAGGGAC TGTAGATTTA 1080  
ATGATGCGTT TTCAAGAATA CACACCAAAA CAATATGTCA GCTTCCCTTT GGCCTGCAGT 1140  
TTGTACCAA TCCTTAATTT TTCCTGAATG AGCAAGCTTC TCTTAAAAGA TGCTCTCTAG 1200  
15 TCATTTGGTC TCATGGCAGT AAGCCTCATG TATACTAAGG AGAGTCTTCC AGGTGTGACA 1260  
ATCAGGATAT AGAAAAACAA ACGTAGTGTN TGGGATCTGT TTGGAGACTG GGATGGGAAC 1320  
20 AAGTTCATTT ACTTAGGGGT CAGAGAGTCT CGACCAGAGG AGGCCATTCC CAGTCCTAAT 1380  
CAGCACCTTC CAGAGACAAG GCTGCAGGCC CTGTGAAATG AAAGCCAAGC AGGAGCCTTG 1440  
GNTCTGAGGC ATCCCCAAAG TGTAACGTAG AAGCCTTGCA TCCTTTTCTT GTGTAAAGTA 1500  
25 TTTATTTTGT TCAAATTGCA GGAAACATCA GGCACCACAG TGCATGAAAA ATCTTTCACA 1560  
GCTAGAAATT GAAAGGGCCT TGGGTATAGA GAGCAGCTCA GAAGTCATCC CAGCCCTCTG 1620  
30 AATCTCCTGT GCTATGTTTT ATTTCTTACC TTAAATTTTT CCAGCATTTC CACCATGGGC 1680  
ATTCAGGCTC TCCACACTCT TCACTATTAT CTCTTGGTCA GAGGACTCCA ATAACAGCCA 1740  
GGTTTACATG AACTGTGTTTT GTTCATTCTG ACCTAAGGGG TTTAGATAAT CAGTAACCAT 1800  
35 AACCCCTGAA GCTGTGACTG CCAAACATCT CAAATGAAAT GTTGTGGCCA TCAGAGACTC 1860  
AAAAGGAAGT AAGGATTTTA CAAGACAGAT TAAAAAATAA TTGTTTTGTC CAAATATAG 1920  
40 TTGTTGTGTA TTTTTTTTTA AGTTTTCTAA GCAATATTTT TCAAGCCAGA AGTCCTCTAA 1980  
GTCTTGCCAG TACAAGGTAG TCTTGGAAG AAAAGTTGAA TACTGTTTTG TTTTCATCTC 2040  
AAGGGGTTC CTGGGTCTTG AACTACTTTA ATAATAACTA AAAAACCCT TCTGATTTTC 2100  
45 CTTCACTGAT GTGCTTTTGG TGAAAGAATT AATGAAGTCC AGTACCTGAA AGTGAAAGAT 2160  
TTGATTTTGT TTCCATCTTC TGTAATCTTC CAAAGAATTA TATCTTTGTA AATCTCTCAA 2220  
50 TACTCAATCT ACTGTAAGTA CCCAGGGAGG CTAATTTCTT TAAAAAATAA AAAAAAAA 2278

55 (2) INFORMATION FOR SEQ ID NO: 79:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1143 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

60

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

5    CCCCCTCCAAC TCTCAACCCA CTTCTCCAGC CAGCGCCCCA GCCCTCCCCG CGCCCGCTCG    60  
      CAGGTCCCGA GGAGCGCAGA CTGTGTCCCT GACAATGGGA ACAGCCGACA GTGATGAGAT    120  
      GGCCCCGGAG GCCCCACAGC ACACCCACAT CGATGTGCAC ATCCACCAGG AGTCTGCCCT    180  
 10    GGCCAAGCTC CTGCTCACCT GCTGCTCTGC GCTGCGGCCC CGGGCCACCC AGGCCAGGGG    240  
      CAGCAGCCGG CTGCTGGTGG CCTCGTGGGT GATGCAGATC GTGCTGGGGA TCTTGAGTGC    300  
 15    AGTCCTAGGA GGATTTTCTT ACATCCGCGA CTACACCTTC CTCGTACACT CGGGAGCTGC    360  
      CATCTGGACA GGGGCTGTGG CTGTGCTGGC TGGAGCTGCT GCCTTCATTT ACGAGAAACG    420  
      GGGTGGTACA TACTGGGCCC TGCTGAGGAC TCTGCTAGCG CTGGCAGCTT TCTCCACAGC    480  
 20    CATCGCTGCC CTCAAACCTT GGAATGAAGA TTTCCGATAT GGCTACTCTT ATTACAACAG    540  
      TGCCTGCCGC ATCTCCAGCT CGAGTGA CTG GAACACTCCA GCCCCCACTC AGAGTCCAGA    600  
 25    AGAAGTCAGA AGGCTACACC TATGTACCTC CTTTCATGGAC ATGCTGAAGG CCTTGTTTCAG    660  
      AACCTTCAG GCCATGCTCT TGGGTGTCTG GATTCTGCTG CTTCTGGCAT CTCTGGCCCC    720  
      TCTGTGGCTG TACTGCTGGA GAATGTTCCC AACCAAAGGG AAAAGAGACC AGAAGGAAAT    780  
 30    GTTGGAAGTG AGTGAATCT AGCCATGCCT CTCCTGATTA TTAGTGCCTG GTGCTTCTGC    840  
      ACCGGGCGTC CCTGCATCTG ACTGCTGGAA GAAGAACCAG ACTGAGGAAA AGAGGCTCTT    900  
 35    CAACAGCCCC AGTTATCCTG GCCCCATGAC CGTGGCCACA GCCCTGCTCC AGCAGCACTT    960  
      GCCCATTCTT TACACCCCTT CCCCATCCTG CTCGCTTCA TGTCCCCTCC TGAGTAGTCA    1020  
      TGTGATAATA AACTCTCATG TTATTGTTNN NAAAAAAAAA AAAAAAAAAA AATTTGGGGG    1080  
 40    GGGGCCGGTA CCCATTGGGC CTNNGGGGN GGTTTAAAT TAATGGGGG GGTTTAAAG    1140  
      GGN    1143

45

(2) INFORMATION FOR SEQ ID NO: 80:

50    (i) SEQUENCE CHARACTERISTICS:  
      (A) LENGTH: 557 base pairs  
      (B) TYPE: nucleic acid  
      (C) STRANDEDNESS: double  
      (D) TOPOLOGY: linear

55    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

     GGCAGAGAGC AGATGGCCTT GACACCAGCA GGGTGACATC CGCTATTGCT ACTTCTCTGC    60  
 60    TCCCCACAG TTCCTCTGGA CTTCTCTGGA CCACAGTCCT CTGCCAGACC CCTGCCAGAC    120

225

5 CCCAGTCCAC CATGATCCAT CTGGGTCACA TCCTCTTCCT GCTTTTGCTC CCAGTGGCTG 180  
 CAGCTCAGAC GACTCCAGGA GAGAGATCAT CACTCCCTGC CTTTACCCT GGCACCTCAG 240  
 GCTCTTGTTT CGGATGTGGG TCCCTCTCTC TGCCGCTCCT GGCAGGCCTC GTGGCTGCTG 300  
 ATGCGGTGGC ATCGCTGCTC ATCGTGGGGG CGGTGTTCCT GTGCGCACGC CCACGCCGCA 360  
 10 GCCCCGCCCA AGAAGATGGC AAAGTCTACA TCAACATGCC AGGCAGGGGC TGACCCTCCT 420  
 GCAGCTTGA CTTTGA CTGACCCTCT CATCCTGGAT GGTGTGTGGT GGCACAGGAA 480  
 CCCCCGCCCC AACTTTTGA TTGTAATAAA ACAATTGAAA CACCAAAAAA AAAAAAAAAA 540  
 15 AAAAAAAAAA AANTCGA 557

20

(2) INFORMATION FOR SEQ ID NO: 81:

25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 795 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

GCGGGGGCGA TGTGGAGCGC GGGCCGCGGC GGGGCTGCCT GGCCGGTGCT GTTGGGGCTG 60  
 CTGCTGGCGC TGTTAGTGCC GGGCGGTGGT GCCGCCAAGA CCGGTGCGGA CTCGTGACCT 120  
 35 GCGGGTCGGT GCTGAAGCTG CTCAATACGC ACCACCGCGT GCGCTGCACT CGCAGACAT 180  
 CAAATACGGA TCCGGCAGCG GCCAGCAATC GGTGACCGC GTAGAGGCGT CGGACGACGC 240  
 40 MAATAGCTAC TGGCGGATCC GCGGCGGCTC GGAGGGCGGG TGCCCGCGCG GTCCCCGGT 300  
 GCGCTGCGGG CAGGCGGTGA GGCTCACGCA TGTSCTTACG GGCAAGAACY TGCACACGCA 360  
 CCAVTTCCCG TCGCCGCTGT CCAACAACCA GGAGGTGAGT GCCTTTGGGG AAGACGGCGA 420  
 45 GGGCGACGAC CTGGACCTAT GGACAGTGCG CTGCTCTGGA CAGCACTGGG AGCGTGAGGC 480  
 TGCTGTGCCT TCCAGCATGT GGGCACCTCT GTGTTCTGT CAGTCACGGG TGAGCAGTAT 540  
 GGAAGCCCCA TCCGTGGGCA GCATGAGGTC CACGGCATGC CCAGTGCCAA CACGCACAAT 600  
 50 ACGTGAAGG CCATGAAGG CATCTTCATC AAGCCTAGTG TGGAGCCCTC TGCAGGTCAC 660  
 GATGAACCTCT GAGTGTGTGG ATGGATGGGT GGATGGAGCG TGGCAGGTGG GGCCTCTGCA 720  
 55 GGGCCACTCT TGGCAGAGAC TTTGGGTTTG TAGGGTCCT CAAGTGCCTT TGTGATTAA 780  
 GAATGTTGGT CTATG 795

60

## (2) INFORMATION FOR SEQ ID NO: 82:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1324 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

NAGGCTTTAA AGCGCTACC CTGCCTGCAG GTGAGCAGTG GTGTGTGAGA GCCAGGCGTC 60  
CCTCTGCCTG CCCACTCAGT GGCAACACCC GGGAGCTGTT TTGTCTTTTG TGGAGCCTCA 120  
15 GCAGTTCCCT CTTTCAGAAC TCACTGCCAA GAGCCCTGAA CAGGAGCCAC CATGCAGTGC 180  
TTCAGCTTCA TTAAGACCAT GATGATCCTC TTCAATTTGC TCATCTTTCT GTGTGGTGCA 240  
20 GCCCTGTTGG CAGTGGGCAT CTGGGTGTCA ATCGATGGGG CATCCTTTCT GAAGATCTTC 300  
GGGCCACTGT CGTCCAGTGC CATGCAGTTT GTCAACGTGG GCTACTTCCT CATCGCAGCC 360  
GGCGTTGTGG TCTTTGCTCT TGGTTTCCTG GGCTGCTATG GTGCTAAGAC TGAGAGCAAG 420  
25 TGTGCCCTCG TGACGTTCTT CTTATCCTC CTCCTCATCT TCATTGCTGA GGTTCAGCT 480  
GCTGTGGTCG CCTTGGTGTA CACCACAATG GCTGAGCACT TCCTGACGTT GCTGGTAGTG 540  
30 CCTGCCATCA AGAAAGATTA TGGTTCCAG GAAGACTTCA CTCAAGTGTG GAACACNACC 600  
ATGAAAGGGC TCAAGTGCTG TGGCTTCACC AACTATACGG ATTTTGAGGA CTCACCCTAC 660  
TTCAAAGAGA ACAGTGCCTT TCCCCATTG TGTGCAATG ACAACGTCAC CAACACAGCC 720  
35 AATGAAACCT GCACCAAGCA AAAGGCTCAC GACCAAAAAG TAGAGGGTGT CTTCAATCAG 780  
CTTTGTATG ACATCCGAAC TAATGCAGTC ACCGTGGGTG GTGTGGCAGC TGGGAATTGGG 840  
40 GGCTCGAGC TGGCTGCCAT GATTGKTCC ATGTATCTGT ACTGCAATCT ACAATAAGTC 900  
CACTTCTGCC TCTGCCACTA CTGCTGCCAC ATGGGAACTG TGAAGAGGCA CCCTGGCAAG 960  
CAGCAGTGAT TGGGGGAGGG GACAGGATCT AACAAATGTCA CTGGGCCAG AATGGACCTG 1020  
45 CCTTTCTGC TCCAGACTG GGGCTAGATA GGGACCACTC CTTTTCAGGA TGCCTGACTT 1080  
TCCTTCCATT GGTGGGTGGA TGGGTGGGGG GCATTCCAGA GCCTCTAAGG TAGCCAGTTC 1140  
50 TGTGCCCCAT TCCCCAGTC TATTAAACCC TTGATATGCC CCTAGGCCT AGTGGTGATC 1200  
CCAGTGCTCT ACTGGGGGAT GAGAGAAAGG CATTTTATAG CCTGGGCATA AGTGAAATCA 1260  
GCAGAGCCTC TGGGTGGATG TGTAGAAGGC ACTTCAAAT GCATAAACCT GTTACAATGT 1320  
55 TAAA 1324



## (2) INFORMATION FOR SEQ ID NO: 83:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1494 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

10 CTCAGGCTTC TGTCTCACTT TTCCGGGGGG GGGATTAGGG CAAGGAGGGC ATGAGGGACT 60  
 GTCTCTCCCT AAAACCCAGA CCCCTGTTCC CCACTCAGTT CTCTTCATC CTCTCCTCA 120  
 15 TCTTCATTGC TGAGGTTGCA GCTGCTGTGG TCGCCTTGGT GTACACCACA ATGGTGAGAC 180  
 ACTGGGATGG AGGAAGGGAA GAAGATTGGG CAAAACCTG GGAGTGGGCT GTGGCCTGTG 240  
 AATGGCCACC TTCTGTACCA GCCCCTAAAC ACTGGCCTGC CTCACCCAGG CTGAGCACTT 300  
 20 CCTGACGTTG CTGGTAGTGC CTGCCATCAA GAAAGATTAT GGTTCCCAGG AAGACTTCAC 360  
 TCAAGTGTGG AACACCACCA TGAAAGGGGT AAGGTTGGCT GGGGAGGTT TTAGGGTGGA 420  
 25 GAGAAAGAAG CAAGGCCCA CCTCCACCT CATCTGTCT CCAGCTCAAG TGCTGTGGCT 480  
 TCACCAACTA TACGGATTTT GAGGACTCAC CCTACTTCAA AGAGAACAGT GCCTTTCCCC 540  
 CATTTCTGTG CAATGACAAC GTCACCCAAC ACAGCCCAAT GAAACCTGCA CCAAGCAAAA 600  
 30 GGCTCACSAC CNAAAARTAN AGGTGTGGGC TGGCATGAGT GGGTGGGGAC TGTTTTCATG 660  
 GCCTCAGAGT GGCAAACGGG GATGGGAGTA GGCAGCTGC CAACTATAAA TGCTCTTTTC 720  
 35 TCTTCCYGA GGGTGTCTC AATCAGCTTT TGTATGACAT CCGAACTAAT GCAGTCACCG 780  
 TGGGTGGTGT GGCAGCTGGA ATTGGGGGCC TCGAGGTAAG CAGATSAGGA GCTGGGACTG 840  
 GGACATGGGC ATGAGACCAG GGCTGCTCAA CCCATCTGAG GCCTCTCTGG AGGAAACAGA 900  
 40 CTCTAACTG GGCTCAGGT AGGGTGTCTG TGGGACAGGC TTCAGGATCC CTATCATGTT 960  
 CCCTCATCTC TCCCTGTTCC TCCCTCTCCA GCTGGCTGCC ATGATTGTGT CCATGTATCT 1020  
 45 GTACTGCAAT CTACAATAAG TCCACTTCTG CCTCTGCCAC TACTGCTGCC ACATGGGAAC 1080  
 TGTGAAGAGG CACCCTGGCA AGCAGCAGTG ATTGGGGGAG GGGACAGGAT CTAACAATGT 1140  
 CACTTGGGCC AGAATGGACC TGCCCTTTCT GCTCCAGACT TGGGGCTAGA TAGGGACCAC 1200  
 50 TCCTTTTAGC GATGCCTGAC TTTCTTTCCA TTGGTGGGTG GATGGGTGGG GGGCATTCCA 1260  
 GAGCCTCTAA GGTAGCCAGT TCTGTGCCCC ATTCCCCCAG TCTATTAAAC CTTGATATG 1320  
 55 CCCCTAGGC CTAGTGGTGA TCCAGTGCT CTAAGGGGG ATGAGAGAAA GGCATTTTAT 1380  
 AGCCTGGGCA TAAAGTAAAT CAGCAGAGCC TCTGGGTGGA TGTGTAGAAG GCACTTCAAA 1440  
 ATGCATAAAC CTGTTACAAT GTTAAAAAAA AAAAAAAA AACTCGACTC TGCC 1494  
 60

## (2) INFORMATION FOR SEQ ID NO: 84:

5

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1285 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

10

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

15 GCTACGTGGC TGGCATGCAT GGAACGAGG CCCTGGGGCG GGAGTTGCTT CTGCTCCTGA 60  
TGCAGTTCCT GTGCCATGAG TTCCTGCGAG SGAACCCACG GGTGACCCGG CTGCTCTCTG 120  
AGATGCGCAT TCACCTGCTG CCCTCCATGA ACCCTGATGG CTATGAGATC GCCTACCACC 180  
20 GGGGTTTCTG RCTGGTGGGC TGGGCCGARG GCCGCTGGAA CAACCAGAGC ATCGATCTTA 240  
ACCATAATTT TGCTGAMCTC AACACACCAC TGTGGGAAGC ACAGGACGAT GGAAGGTGC 300  
CCACATCGT CCCCAACCAT CACCTGCCAT TGCCCACTTA CTACACCCTG CCCAATGCCA 360  
25 CCGTGGCTCC TGAAACGCGG GCAGTAATCA AGTGGATGAA GCGGATCCCC TTTGTGCTAA 420  
GTGCCAACCT CCACGGGGGT GAGCTCGTGG TGTCTTACCC ATTGACATG ACTCGCACCC 480  
30 CGTGGGCTGC CCGCGAGCTC ACGCCACAC CAGATGATGC TGTGTTTCGC TGGCTCAGCA 540  
CTGTCTATGC TGGCAGTAAT CTGGCCATGC AGGACACCAG CCGCCGACCC TGCCACAGCC 600  
AGGACTTCTC CGTGCACGGC AACATCATCA ACGGGGCTG ACTNGGCACA CCGTCCCCGG 660  
35 GANGCATGAA TGAYTTCAGC TACCTACACA CCAACTGCTT TGAGGTCACT GTGGAGCTGT 720  
SCTGTGACAA GTTCCCTCAC GAGAATGAAT TGCCCCAGGA GTGGGAGAAC AACAAAGACG 780  
40 CCCTCCTCAC CTACCTGGAG CAGGTGCGCA TGGGCATTGC AGGAGTGGTG AGGGACAAGG 840  
ACACGGAGCT TGGGATTGCT GACGCTGTCA TTGCCGTGGA TGGGATTAAC CATGACGTGA 900  
CCACGGCGTG GGGCGGGGAT TATTGGCGTC TGCTGACCCC AGGGGACTAC ATGGTGA CTG 960  
45 CCAGTKCCGA GGGCTACCAT TCAGTGACAC GGAAGTGTG GTTACCTTTT GAAGAGGGCC 1020  
CCTTCCCCCTG CAATTTCTGT CTCACCAAGA CTCCCAAACA GAGGCTGCGC GAGCTGCTGG 1080  
50 CAGCTGGGGC CAAGGTGCCC CCGACCTTC GCAGGCGCCT GGAGCGGCTA AGGGGACAGA 1140  
AGGATTGATA CCTGCGGTTT AAGAGCCCTA GGCAGGCTG GACCTGTCAA GACGGGAAGG 1200  
GGAAGAGTAG AGAGGGAGGG ACAAAGTGAG GAAAAGGTGC TCATTAAAGC TACCGGGCAC 1260  
55 CTTAAAAAAA AAAAAAAAAA AAAAA 1285

60

## (2) INFORMATION FOR SEQ ID NO: 85:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 394 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

10 GCGCGCTCTA GGAAGTAGTG GATCCCCCGG GNCTGCAGGT GTGGAGTGGG CCATCGTAAA 60  
 TAGTATCTGT GCATAAGGTG GTTGTGCGAT AAATGAGTTA ATGTATGCAA AGCCCTTGGC 120  
 15 CCAGAGCCGG CGCAGAGCAT TGTGTAAGTS CTGGCAGGCG TCATGATGGA GATATCATGT 180  
 CTCCTCTTCT TGATTCAGGA TTCTGATGAG ATGGAGGATG GGCCTGGGGT TCAGGATTAG 240  
 GCCTTGAGGC ACTGCTCCAG CCTCCTTTGT GGGCCCTGTC ACCCTTGGCT TCATCGGGCC 300  
 20 GTARCAAGTC TCCCCTCTCC CACTYTGAG CAGARGTGT CAAGAACTGC CTGCTCACGG 360  
 TTCGTGTTCT GCAAGGCCAT CGCCTAACCT CTAA 394  
 25

## (2) INFORMATION FOR SEQ ID NO: 86:

## (i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 1925 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 35 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

AGTGAAGGGA GCTGGCCGTG CGACTGGGCT TCGGCCCTG TGCCAGAGGA GCANGCCTTC 60  
 40 CTGAGCAGGA GGAAGCAGGT GGTGGCCCGG GCCTTGAGGC AGGCCCTGCA GCTGGATGGA 120  
 GACCTGCAGG AGGATGAGAT CCCAGTGGTA GCTATTATGG CCACTGGTGG TGGGATCCGG 180  
 GCAATGACTT CCCTGTATGG GCAGCTGGCT GGCCTGAAGG AGCTGGGCCT CTGGAATTGC 240  
 45 KTCTCCTACA TCACCGGGG CTGGGGCTCC ACCTGGGCCT TGGCCAACCT TTATAAGGAC 300  
 CCAGAGTGGT CTCAGAAGGA CTTGGCAGGG CCCACTGAGT TGCTGAAGAC CCAGGTGACC 360  
 50 AAGAACAAGC TGGGTGTGCT GGCCCCCAGC CAGCTGCAGC GGTACCGCA GGAGCTGGCC 420  
 GAGCGTGCCC GCTTGGGCTA CCCAAGCTGC TTCACCAACC TGTGGGCCCT CATCAACGAG 480  
 GCGCTGCTGC ATGATGAGCC CCATGATCAC AAGCTCTCAG ATCAACGGGA GGCCTGAGT 540  
 55 CATGGCCAGA ACCCTCTGCC CATCTACTGT GCCCTCAACA CCAAAGGCA GAGCCTGACC 600  
 ACTTTTGAAT TTGGGGAGTG GTGCGAGTTC TCTCCCTACG AGGTCGGCTT CCCCAAGTAC 660  
 60 GGGGCCTTCA TCCCCTCTGA GCTCTTTGGC TCCGAGTTCT TTATGGGGCA GCTGATGAAG 720

5 AGGCTTCCTG AGTCCCGCAT CTGCTTCTTA GAAGGTATCT GGAGCAACCT GTATGCAGCC 780  
 AACCTCCAGG ACAGCTTATA CTGGGCCTCA GAGCCAGCC AGTTCTGGGA CCGCTGGGTC 840  
 AGGAACCAGG CCAACCTGGA CAAGGAGCAG GTCCCCCTTC TGAAGATAGA AGAACCACCC 900  
 TCAACAGCCG GCAGAATAGC TGAGTTTTC ACCGATCTTC TGACGTGGCG TCCACTGGCC 960  
 10 CAGGCCACAC ATAATTTCCT GCGTGGCCTC CATTTCCACA AAGACTACTT TCAGCATCCT 1020  
 CACTTCTCCA CATGGAAAGC TACCACTCTG GATGGGCTCC CCAACCAGCT GACACCCTCG 1080  
 15 GAGCCCCACC TGTGCCTGCT GGATGTTGGC TACCTCATCA ATACCAGCTG CCTGCCCCCTC 1140  
 CTGCAGCCCA CTCGGGACGT GGACCTCATC CTGTCAITGG ACTACAACCT CCACGGAGCC 1200  
 TTCCAGCAGT TGCAGCTCCT GGGCCGGTTC TGCCAGGAGC AGGGGATCCC GTTCCCACCC 1260  
 20 ATCTCGCCCA GCCCCGAAGA GCAGCTCCAG CCTCGGGAGT GCCACACCTT CTCCGACCCC 1320  
 ACCTGCCCCG GAGCCCTGTC GGTGCTGCAC TTTCTCTGG TCAGCGACTC CTTCCGGGAG 1380  
 TACTCGGCCC CTGGGGTCCG GCGGACACCC GAGGAGGCGG CAGCTGGGGA GGTGAACCTG 1440  
 25 TCTTCATCGG ACTCTCCCTA CCACTACACG AAGGTGACCT ACAGCCAGGA GGACGTGGAC 1500  
 AAGCTGCTGC ACCTGACACA TTACAATGTC TGCAACAACC AGGAGCAGCT GCTGGAGGCT 1560  
 30 CTGCGCCAGG CAGTGCAGCG GAGGCGGCAG CGCAGGCCCC ACTGATGGCC GGGGCCCCCTG 1620  
 CCACCCTAA CTCTCATTCA TTCCCTGGCT GCTGAGTTGC AGGTGGGAAC TGTATCACG 1680  
 35 CAGTGCTTCA GAGCCTCGGG CTCAGGTGGC ACTGTCCCAG GGTCCAGGCT GAGGGCTGGG 1740  
 AGCTCCCTTG CGCCTCAGCA GTTTCAGTG GGGTAAGGAG GCCAAGCCCA TTTGTGTAAT 1800  
 CACCCAAAAC CCCCCGGCCT GTGCCTGTTT TCCCTTCTGC GCTACCTTGA GTAGTTGGAG 1860  
 40 CACTTGATAC ATCACAGACT CATAAAATG TGAGGCGCTG AGAAAAAAA AAAAAAAA 1920  
 CTCGA 1925

45

(2) INFORMATION FOR SEQ ID NO: 87:

50 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1818 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

CCGGGCCCCC CCNCGNGNTT TTTTTTTTTT TTTTTTTTTT TATGAGTCTG TRATGTATCA 60  
 60 AGTGCTCCAA CTAICTAAGG TAGCGCAGAA GGGAAACAG GCACAGGCCG GGGGGTTTTG 120

	GGTGATTACA CAAATGGGCT TGGCCTCCTT ACCCCACTGC AAAGTGTGA GGCACAAGGG	180
	AGCTCCCAGC CCTCAGCCTG GACCTGGGA CAGTGCCACC TGAGCCCGAG GCTCTGNAAG	240
5	CACTGCGTGA TGACAGTTCC CACCTGCAAC TCAGCAGCCA GGAATGAAT GAGAGTTAGG	300
	GGTGGCAGGG GCCCCGGCCA TCAGTGGGGC CTGCGCTGCC GCCTCCGCTG CACTGCCTGG	360
10	CGCAGAGCCT CCAGCAGCTG CTCCTGGTTG TTGCAGACAT TGTAATGTGT CAGGTGCAGC	420
	AGCTTGTCCA CGTCCTCCTG GCTGTAGGTC ACCTTCGTGT AGTGGTAGGG AGAGTCCGAT	480
	GAAGACAGGT TCACCTCCCC AGCTGCCGCC TCCTCGGGTG TCCGCCGGAC CCCAGGGGCC	540
15	GAGTACTCCC GGAAGGAGTC GCTGACCAGA GGAAAGTGCA GCACCGCAGG GGCTCCGGGG	600
	CAGGTGGGGT CGGAGAAGGT GTGGCACTCC CGAGGCTGGA GCTGCTCTTC GGGGCTGGGC	660
20	GAGATGGGTG GGAACGGGAT CCCCTGCTCC TGGCAGAACC GGCCAGGAG CTGCAACTGC	720
	TGGAAGGCTC CGTGGAGGTT GTAGTCCAAT GACAGGATGA GTTCCACGTC CCGAGTGGGC	780
	TGCAGGAGGG GCAGGCAGCT GGTATTGATG AGGTAGCCAA CATCCAGCAG GCACAGGTGG	840
25	GGCTCCGAGG GTGTCAGCTG GTTGGGGAGC CCATCCAGAG TGGTAGCTTT CCATGTGGAG	900
	AAGTGAGGAT GCTGAAAGTA GTCTTTGTGG AAATGGAGGC CACGCAGGAA ATTATGTGTG	960
30	GCCTGGGCCA GTGGACGCCA CGTCAGAAGA TCGGTGAAAA ACTCAGCTAT TCTGCCGGCT	1020
	GTTGAGGGTG GTTCTTCTAT CTTCAGAAGG GGGACCTGCT CCTGTGCCAG GTTGGCCTGG	1080
	TTCTTGACCC AGCGGTCCCA GAACTGGCTG GGCTCTGAGG CCCAGTATAA GCTGTCTGG	1140
35	AGGTTGGCTG CATAAGGTT GCTCCAGATA CCTTCTAAGA AGCAGATGCG GGAAGTCAAG	1200
	AGCTCTTCA TCAGCTGCCC CATAAAGAAC TCGGAGCCAA AGAGCTCAGA GGGGATGAAG	1260
40	GCCCCGTACT TGGGAAGCC GACCTCGTAG GGAGAGAACT CGCACCCTC CCCAAATTCA	1320
	AAAGTGGTCA GGCTCTGCCC TTTGGTGTG AGGGCACAGT AGATGGGCAG AGGGTTCTGG	1380
	CCATGACTCA GGGCCTCCCG TTGATCTGAG AGCTTGTGAT CATGGGGCTC ATCATGCAGC	1440
45	AGCGCTCGT TGATGAGGGC CCACAGGTTG GTGAAGCAGC TTGGGTAGCC CAAGCGGGCA	1500
	CGCTCGGCCA GCTCCTGCCG GTACCGCTGC AGCTGGCTGG GGGCCAGCAC ACCCAGCTTG	1560
50	TTCTTGGTCA CCTGGGTCTT CAGCAACTCA GTGGGCCCTG CCAGGTCCTT CTGAGACCAC	1620
	TCTGGGTCTT YATAAAGGTT GGCCAAGGCC CAGGTGGAGC CCGAGGCCCC GGTGATGTAG	1680
	GAGACGCAAT CCAAGAGGCC CCAGCTCCTT TCAGGCCAGC CAGCTGCCCA TACAGGGAAG	1740
55	TCATTGCCCG GATCCCACCA CCAGTGGCCA TAATAGCTAC CACTGGGATC TCATCCTCCT	1800
	GCAGGTCTCC ATCCAGCT	1818

## (2) INFORMATION FOR SEQ ID NO: 88:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 539 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

10 AGGGTAATTA ATATGAAGTG CAAAAAGTTG AATGTTCCAG TCTAAAAGGC AGTGGGAGAA 60  
 ATTACATAGC ATGGAAATAA TAAAATGAAY TCTTATTAAT GAGAACGAGG YTCTTGCACT 120  
 15 GGCAAGTTCT GCTGGTCACC CGATGGGGAT GGGAGCCTTT CAAGCTTTTT TTTGGGTAAT 180  
 ACTCACAGTT TCCAACGTCT GTGTACTTTT CAAAATGAGC TTGTTCTTCC TTCTGACACT 240  
 20 CATCTCAAAG CTCCATGGTG ACGCAGAGGT CTGTTGAAGG TCACAGGGTC CTCGCTTGCA 300  
 TTGGCATAAG GTCTGTAGC ATCACTTGTT AGCCCACTGC TGCTTGAAGG AACTAAGAGT 360  
 ATTCAGGGAT AGAGAGCTGA AAATAGGATT AATTNNTTCC TTTTGACTCT CCCCTCAAGA 420  
 25 TGTCCTTGCT TTGGTCTGAA AACCTCTCCT GACAACTTT GCCCAAAGCA AACCATCTGC 480  
 CTTTCTGAA CTCTGAGTGA ATATATTAGC ATCTTCCCTT CTGAGCCCTC GTACTGCCA 539  
 30

## (2) INFORMATION FOR SEQ ID NO: 89:

## (i) SEQUENCE CHARACTERISTICS:

- 35 (A) LENGTH: 855 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

40 CCTCTGCCCA GGCGCACCC GAGCTCAGGC TCGTGCCAC CCACCAAGTT CCAGTGCCGC 60  
 45 ACCAGTGGCT TATGCGTGCC CCTCACCTGG CGTGCGACA GGNACTTGGA CTGCAGCGAT 120  
 GGCAGCGATG AGGAGGAGTG CAGGATTGAG CCATGTACCC AGAAAGGGCA ATGCCACCG 180  
 50 CCCCCTGGCC TCCCCTGCCC CTGCACCGGC GTCAGTGACT GCTCTGGGG AACTGACAAG 240  
 AAAGTGGCA ACTGCAGCCG CCTGGCTGTC CTAGCAGCG AGCTCCGTTG CACGCTGAGC 300  
 GATGACTGCA TTCCACTCAC GTGGCGCTGC GACGGCCACC CAGACTGTCC CGACTCCAGC 360  
 55 GACGAGCTCG GCTGTGGAAC CAATGAGATC CTCCCGGAAG GGGATGCCAC AACCATGGGG 420  
 CCCCCTGTGA CCCTGGAGAG TGTACCTCT CTCAGGAATG CCACAACCAT GGGGCCCCCT 480  
 60 GTGAACCCTG GAGAGTGTC CCTCTGTGG GAATGCCACA TCCTCTCTG CCGGAGACCA 540

GTCTGGAAGC CCAACTGCCT ATGGGGTTAT TGCAGCTGCT GCGGTGCTCA GTGCAAGCCT 600  
GGTCACCGCC ACCCTCCTCC TTTGTCTCTG GCTCCGAGCC CAGGAGCGCC TCCGCCCACT 660  
5 GGGGTTACTG GTGGCCATGA AGGAGTCCCT GCTGCTGTCA GAACAGAAGA CCTCGCTGCC 720  
CTGAGGACAA GCACTTGCCA CCACCGTCAC TCAGCCCTGG GCGTACNGSA CAGGAGGAGA 780  
10 GCAGTGATGC GGATGGGTAC CGGGCACACC AGCCCTTCAG AGACCTGAGC NCTTCTGGCC 840  
ACTGGAACCTT CGAAC 855

15

(2) INFORMATION FOR SEQ ID NO: 90:

(i) SEQUENCE CHARACTERISTICS:  
20 (A) LENGTH: 628 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

AAGGACGTGC CGTGCCGCTG GGTCTGAGC CGGAGTGGTC GGTGGGTGGG ATGGAGGCGA 60  
CCTTGGAGCA GCACTTGGA GACACAATGA AGAATCCCTC CATGTGTTGA GTCCTGTGCA 120  
30 CAGATTCACA AGGACTTAAT CTGGGTGACC GCGGGACCCT GTCAGATGAG CATGCTGGAG 180  
TGATATCTGT TCTAGCCCAG CAAGCAGCTA AGCTAACCTC TGACCCCACT GATATTCCTG 240  
TGGTGTGTCT AGAATCAGAT AATGGGAACA TTATGATCCA GAAACACGAT GGCATCACGG 300  
35 TGGCAGTGCA CAAAATGGCC TCTTGATGCT CATATCTGTT CTTGAGCAGC CTGTCATAGG 360  
AACTGGATCC TACCTATGTT AATTACCTTA TAGAACTACT AAAGTTCAG TAGTTAGGCC 420  
40 ATTCATTTAA TGTGCATTAG GCACTTTTCT GTTTATTTAA GAGTCAATTG CTTTCTAATG 480  
CTCTATGGAC CGACTATCAA GATATTAGTA AGAAAGGATC ATGTTTGA GACAGGATC 540  
CAGGTCACTT TGTATATAGA ATTTGCTGT ATTCAATAAA TCTGTTTGA GGNAAAAAAA 600  
45 AAAAAA AAAA AAMTSAGGG CCGAAGCT 628

50

(2) INFORMATION FOR SEQ ID NO: 91:

(i) SEQUENCE CHARACTERISTICS:  
55 (A) LENGTH: 1053 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

	CTCTTTTCTG CAGTTCAAGG GAAAGACGAG ATCTTGCA CA AGGCACTCTG CTTCTGCCCT	60
	TGGCTGGGGA AGGGTGGCAT GGARCTCTC CGGCTGCTCA TCTTACTCTT TGTACACAGAG	120
5	CTGTCCGGAG CCCACAACAC CACAGTGTTC CAGGGCGTGG CGGGCCAGTC CCTGCAGGTG	180
	TCTTGCCCCCT ATGACTCCAT GAAGCACTGG GGGAGGCGCA AGGCCTGGTG CCGCCAGCTG	240
10	GGAGAGAAGG GCCCATGCCA GCGTGTGGTC AGCACGCACA ACTTGTGGCT GCTGTCTTC	300
	CTGAGGAGGT GGAATGGGAG CACAGCCATC ACAGACGATA CCCTGGGTGG CACTCTCACC	360
	ATTACGCTGC GGAATCTACA ACCCCATGAT GCGGGTCTCT ACCAGTGCCA GAGCCTCCAT	420
15	GGCAGTGAGG CTGACACCCT CAGGAAGGTC CTGGTGGAGG TGCTGGCAGA CCCCTGGAT	480
	CACCGGGATG CTGGAGATCT CTGGTTCCCC GGGGAGTCTG AGAGCTTCGA GGATGCCCAT	540
20	GTGGAGCACA GCATCTCCAG GAGCCTCTTG GAAGGAGAAA TCCCCTTCCC ACCCACTTCC	600
	ATCCTTCTCC TCCTGGCCTG CATCTTCTC ATCAAGATTC TAGCAGCCAG CGNCTCTGG	660
	GCTGCAGCCT GGCATGGACA GAAGCCAGGG ACACATCCAC CCAGTGA ACT GGACTGTGGC	720
25	CATGACCCAG GGTATCAGCT CCAA ACTCTG CCAGGGCTGA GAGACACGTG AAGGAAGATG	780
	ATGGGAGGAA AAGCCCAGGA GAAGTCCAC CAGGGACCAG CCCAGCCTGC ATACTTGCCA	840
30	CTTGGCCACC AGGACTCCTT GTTCTGCTCT GGCAAGAGAC TACTCTGCCT GAACACTGCT	900
	TCTCCTGGAC CCTGGAAGCA GGGACTGGTT GAGGGAGTGG GGAGGTGGTA AGAACACCTG	960
	ACA ACTTCTG AATATGGAC ATTTTAAACA CTTACAAATA AATCCAAGAC TGT CATATTT	1020
35	AAAAAAAAA AAAAAAAAAA AACNCGAGGG GGG	1053

40 (2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 1075 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

50	GCACGAGCCT GATCCTCTCT TTTCTGCAGT TCAAGGGAAA GACGAGATCT TGCACAAGGC	60
	ACTCTGCTTC TGCCCTTGGC TGGGGAAGGG TGGCATGGAG CCTCTCCGGC TGCTCATCTT	120
55	ACTCTTTGTC ACAGAGCTGT CCGGAGCCCA CAACACCACA GTGTTCAGG GCGTGGCGGG	180
	CCAGTCCCTG CAGGTGTCTT GCCCTATGA CTCCATGAAG CACTGGGGGA GGCGCAAGGC	240
	CTGGTGCCGC CAGCTGGGAG AGAAGGGCCC ATGCCAGCGT GTGGTCAGCA CGCACA ACTT	300
60	GTGGCTGCTG TCCTTCCTGA GGAGGTGGAA TGGGAGCACA GCCATCACAG ACGATACCCT	360



GGGTGGCACT CTCACCATTA CGCTGCGGAA TCTACAACCC CATGATGCGG GTCTCTACCA 420  
 GTGCCAGAGC CTCCATGGCA GTGAGGCTGA CACCCTCAGG AAGGTCCTGG TGGAGGTGCT 480  
 5 GGCAGACCCC CTGGATCACC GGGATGCTGG AGATCTCTGG TTCCCCGGGG AGTCTGAGAG 540  
 CTTTCGAGGAT GCCCATGTGG AGCACAGCAT CTCCAGGAGC CTCTTGGAAG GAGAAATCCC 600  
 10 CTTCCCACCC ACTTCCATCC TTCTCCTCCT GGCCTGCATC TTTCTCATCA AGATTCTAGC 660  
 AGCCAGCGCC CTCTGGGCTG CAGCCTGGCA TGGACAGAAG CCAGGGACAC ATCCACCCAG 720  
 TGAAGTGGAC TGTGGCCATG ACCCAGGGTA TCAGCTCCAA ACTCTGCCAG GGCTGAGAGA 780  
 15 CACGTGAAGG AAGATGATGG GAGGAAAAGC CCAGGAGAAG TCCCACCAGG GACCAGCCCA 840  
 GCCTGCATAC TTGCCACTTG GCCACCAGGA CTCCTTGTTC TGCTCTGGCA AGAGACTACT 900  
 20 CTGCCTGAAC ACTGCTTCTC CTGGACCCTG GAAGCAGGGA CTGGTTGAGG GAGTGGGGAG 960  
 GTGGTAAGAA CACCTGACAA CTTCTGAATA TTGGACATTT TAAACACTTA CAAATAAATC 1020  
 CAAGACTGTC ATATTTAAAA AAAAAAAAAA AAAAAAACN CGAGGGGGGN CCCGG 1075  
 25

(2) INFORMATION FOR SEQ ID NO: 93:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2492 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

35

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

TCCCAGCTCA GCTTCCCACC CTGGGCTTTC CGAGGTGCTK TCGCCGCTGT CCCCACT 60  
 40 GCAGCCATGA TCTCCTTAAC GGACACGCAG AAAATGGAA TGGGATTAAC AGGATTTGGA 120  
 GTGTTTTTCC TGTCTTTTGG AATGATTCTC TTTTGTGACA AAGCACTACT GGCTATTGGA 180  
 45 AATGTTTTAT TTGTAGCCCG CTTGGCTTTT GTAATGGTT TAGAAAGAAC ATTCAGATTC 240  
 TTCTTCCAAA AACATAAAAT GAAAGCTACA GGTTTTTTTC TGGGTGGTGT ATTTGTAGTC 300  
 CTTATTGGTT GGCCTTTGAT AGGCATGATC TTCGAAATTT ATGGATTTT TCTCTGTTC 360  
 50 AGGGGCTTCT TTCCTGTCGT TGTGGCTTTT ATTAGAAGAG TGCCAGTCCT TGGATCCCTC 420  
 CTAAATTAC CTGGAATTAG ATCATTTGTA GATAAAGTTG GAGAAAGCAA CAATATGGTA 480  
 55 TAACAACAAG TGAATTTGAA GACTCATTTA AAATATTGTG TTATTTATAA AGTCATTTGA 540  
 AGAATATCA GCACAAAATT AAATTACATG AAATAGCTTG TAATGTTCTT TACAGGAGTT 600  
 TAAAACGTAT AGCCTACAAA GTACCAGCAG CAAATTAGCA AAGAAGCAGT GAAAACAGGC 660  
 60

	TTCTACTCAA GTGAAC TAAG AAGAAGTCAG CAAGCAA ACT GAGAGAGGTG AAATCCATGT	720
	TAATGATGCT TAAGAACTC TTGAAGGCTA TTTGTGTTGT TTTTCCACAA TGTGCGAAAC	780
5	TCAGCCATCC TTAGAGAACT GTGGTGCCCTG TTTCTTTTCT TTTTATTTTG AAGGCTCAGG	840
	AGCATCCATA GGCATTTGCT TTTTAGAAAT GTCCACTGCA ATGGCAAAAA TATTTCCAGT	900
10	TGCACTGTAT CTCTGGAAGT GATGCATGAA TTCGATTGGA TTGTGTCATT TTAAAGTATT	960
	AAAACCAAGG AAACCCCAAT TTTGATGTAT GGATTACTTT TTTTGTAAA CATGGTTAAA	1020
	ATAAACTTC TGTGGTTCTT CTGAATCTTA ATATTTCAAA GCCAGGTGAA AATCTGAACT	1080
15	AGATATTCTT TGTGGAATA TGCAAAGGTC ATTCTTTACT AACTTTTAGT TACTAAATTA	1140
	TAGCTAAGTT TTGTCAGCAG CATACTCCGG AAAGTCTCAT ACTTCTTGGG AGTCTGCCCT	1200
20	CCTAAGTATC TGTCTATATC ATTCATTACG TGTAAGTATT TAACAAAAAA GCATTCTTGA	1260
	CCATGAATGA AGTAGTTTGT TTCATAGCTT GTCTCATTGA ATAGTATTAT TGAAGATACT	1320
	AAATGATGCA AACCAAATGG ATTTTTCCTA TGTGATGATG TAATTTTCTT TTCTTCTTTC	1380
25	TTTTTTTTAA ATTTTAGCAG TGGCTTATTA TTTGTTTTTC ATAAATTAAA ATAACTTTG	1440
	ATAATGTTTA CTTTAAGACA TGTAACATGT TAAAAGGTTA AACTTATGGC TGTTTTTAAA	1500
30	GGGCTATTCA TTTAATCTGA GTTTTCCCTT ATTTTCAGCT TTTTCTTAGC ATATAATAGT	1560
	CATTAAGCAT GACATATCCT TCATATGATC ACTCATCTTG AGTTAATTAG AAAATACCTG	1620
	AGTTCACGTG CTAAAGTCAT TTTACTGTAA TAACTGACT RTGGTTTCTT AAGAACATGA	1680
35	CACTAAAAAA AAAGTGGTTT TTTTCCACCG TTGCTGATTA TTAGACAGTA GGAAATAGCT	1740
	GTTTTCTTTA GTTTTACAAG ATGTGACAGC TTTAGTGGTA GATGTAGGGA AACATTTCAA	1800
40	CAGCCATAGT ACTATTTGTT TTACCACTGA TTGCACTGTT TTGTTTTTTT AACAGTTGCA	1860
	AAGCTTTTTA ATGCATAAAA GTATAATTGA AATCTGTGGT ATTTATTTAC AAACATGTCT	1920
	ACAAAAATAG ATTACAGCTT ATTTTATTTT TAGTTAAATC TCTTAATACA CAGAGNAACT	1980
45	CCCAATCTTG CTCATCTAAA TAAGGAAAGA CTTGGTGTAT AGTGTGATGG TTTAGTCTTA	2040
	AGGATTAAGA CATTTTTGGT ACTTGCATTT GACTTACGAT GTATCTGTGA AAATGGGATG	2100
50	ATATTGACAA ATGGAGACTC CTACCTCAAT AGTTAATGGA ATAATAAGAG GCTACTGTTG	2160
	TGTCTAATGT TCTTCAAAAA AGTAATATCC TCACTTGGAG AGTGTCAAAT ACATACTTTG	2220
	ACCATTGACT TTATATAAGG TGCCCTGTAG AAMTCTGTTA CACATATTTT TGACCCATAT	2280
55	TTTTCACAAT GTCTTGATAA TTCTACCTTT TTAGAGCAAG AATAGTATCT GCTAATGTAA	2340
	GGGACATCTG TATTTAACTC CTTTGTAGAC ATGAATTTCT ATCAAAATGT TCTTTGCACT	2400
60	GTAACAGAGA TTCCTTTTTT CAATAATCTT AATTCAAAGC ATTATTAGGM CTTGAAAGGG	2460

TTTGRTAATC TCCCCGTCCT TGGTAAAGGT TG

2492

5

(2) INFORMATION FOR SEQ ID NO: 94:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 3058 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

15

ACCCTAAATC AACAGACAAT GGCATTGTCG AAGAGCAACC TGTTAATGAA ATCATGTTAA 60

AAATCAAGGT TTGGCTTCAG TTAAATCAC TTGAGGTATG AAGTTTATCC TGTTTTCCAG 120

20

AGATAAACAT AAGTTGATCT TCCCAAAATA CCATCATTAG GACCTATCAC ACAATATCAC 180

TAGTTTTTTT TGTTTGTTTG TTTTTGTTT TTTTCTTGG TAAAGCCATG CACCACAGAC 240

25

TTCTGGGCAG AGCTGAGAGA CAATGGTCCT GACATAATAA GGATCTTTGA TTAACCCCA 300

TAAGGCATGT GTGTGTATAC AAATATACTT CTCTTTGGCT TTTGACATA GAACCTCAGC 360

TGTTAAACAA GGGGAAATAC ATCAGATCTG CAACACAGAA ATGCTCTGCC TGAAATTTCC 420

30

ACCATGCCTA GGAATCACCC CATTTATCCA GGTCTTTCTG GATCTGTTTA ATCAATAAGC 480

CCTATAATCA CTTGCTAAAC ACTGGGCTTC ATCACCAGG GATAAAAACA GAGATCATTG 540

35

TCTTGACCT CTTGCATCAG CCTATTCAAA ATTATCTCTC TCTCTAGCTT TCCACAAATC 600

CTAAATTTCC TGTCCAAGC CACCCAAATT CTCAGATCTT TTCTGGAACA AGGCAGAATA 660

TAAAATAAAT ATACATTTAG TGGCTTGGGC TATGGTCTCC AAAGATCCTT CAAAATACA 720

40

TCAAGCCAGC TTCATCACT CACTTTACTT AGAACAGAGA TATAAGGGCC TGGGATGCAT 780

TTATTTTATC AATACCAATT TTTGTGGCCA TGGCAGACAT TGCTAATCAA TCACAGCACT 840

45

ATTTCTTATT AAGCCCACTG ATTTCTTCAC AATCCTTCTC AAATTACAAT TCCAAGAGC 900

CGCCACTCAA CAGTCAGATG AACCCAACAG TCAGATGAGA GAAATGAACC CTACTTGCTA 960

TCTCTATCTT AGAAAGCAAA AACAAACAGG AGTTTCCAGG GAGAATGGGA AAGCCAGGGG 1020

50

GCATAAAAGG TACAGTCAGG GGAAAATAGA TCTAGGCAGA GTGCCTTAGT CAGGGACCAC 1080

GGGCGCTGAA TCTGCAGTGC CAACACCAAA CTGACACATC TCCAGGTGTA CCTCCAACCC 1140

55

TAGCCTTCTC CCACAGCTGC CTACAACAGA GTCTCCAGC CTTCTCAGAG AGCTAAAACC 1200

AGAAATTTCC AGACTCATGA AAGCAACCCC CCAGCCTCTC CCCAACCCTG CCGCATTTGC 1260

TAATTTTATG AACACTAGGC TTCTTCTTTC ATGTAGTTCC TCATAAGCAG GGGCCAGAAT 1320

60

ATCTCAGCCA CCTGCAGTGA CATGCTGGA CCCCTGAAAA CCATTCCATA GGAGAATGGG 1380

	TTCCCCAGGC TCACAGTGTA GAGACATTGA GCCCATCACA ACTGTTTTGA CTGCTGGCAG	1440
5	TCTAAAACAG TCCACCCACC CCATGGCACT GCCGCGTGAT TCCCGCGCCA TTCAGAAGTT	1500
	CAAGCCGAGA TGCTGACGTT GCTGAGCAAS AGATGGTGAG CATCAGTGCA AATGCACCAT	1560
	TCAGCACATC AGTCATATGC CCAGTGCAGT TACAAGATGT TGTTTCGGCA AAGCATTTTG	1620
10	ATGGAATAGG GAACTGCAAA TGTATGATGA TTTTGAAAAG GCTCAGCAGG ATTTGTCTTT	1680
	AAACCGACTC AGTGTGTCAT CCCCAGTTAT TTAGAATTAC AGTTAAGAAG GAGAACTTC	1740
15	TATAAGACTG TATGAACAAG GTGATATCTT CATAGTGGGC TATTACAGGC AGGAAAATGT	1800
	TTTAACTGGT TTACAAAATC CATCAATACT TGTGTCATTC CCTGTAAAAG GCAGGAGACA	1860
	TGTGATTATG ATCAGGAAAC TGCACAAAAT TATTGTTTTT AGCCCCGTG TTATTGTCCT	1920
20	TTTGAACGTG TTTTTTTTTT TAAAGCCAA ATTTGTGTTG TATATATTCG TATTCCATGT	1980
	GTTAGATGGA AGCATTTCTT ATCCAGTGTG AATAAAAAGA ACAGTTGTAG TAAATTATTA	2040
25	TAAAGCCGAT GATATTTTAT GGCAGGTTAT TCTACCAAGC TGTGCTTGTT GGTTTTTTCCC	2100
	ATGACTGTAT TGCTTTTATA AATGTACAAA TAGTTACTGA AATGACGAGA CCCTTGTTTG	2160
	CACAGCATTA ATAAGAACCT TGATAAGAAC CATATTCTGT TGACAGCCAG CTCACAGTTT	2220
30	CTTGCTGAA GCTTGGTGCA CCCTCCAGTG AGACACAAGA TCTCTCTTTT ACCAAAGTTG	2280
	AGAACAGAGC TGGTGGATTA ATTAATAGTC TTCGATATCT GGCCATGGGT AACCTCATTG	2340
35	TAATATCAT CAGAATGGGC AGAGATGATC TTGAAGTGTC ACATACACTA AAGTCCAAAC	2400
	ACTATGTCAG ATGGGGGTAA AATCCATTAA AGAACAGGAA AAAATAATTA TAAGATGATA	2460
	AGCAAATGTT TCAGCCCAAT GTCAACCCAG TTAATAAATA AATTAATGCT GTGTAAAATG	2520
40	GTTGAATTAG TTTGCAAACT ATATAAAGAC ATATGCAGTA AAAAGTCTGT TAATGCACAT	2580
	CCTGTGGGAA TGGAGTGTTT TAACCAATTG CCTTTTCTTG TTATCTGAGC TCTCCTATAT	2640
45	TATCATACTC AGATAACCAA ATTAAGAGAA TTAGAATATG ATTTTAAATA CACTTAACAT	2700
	TAAACTCTTC TAACTTTCTT CTTTCTGTGA TAATTCAGAA GATAGTTATG GATCTTCAAT	2760
	GCCTCTGAGT CATTGTTATA AAAAATCAGT TATCACTATA CCATGCTATA GGAGACTGGG	2820
50	CAAAACCTGT ACAATGACAA CCCTGGAAGT TGCTTTTTTTT AAAAAAATAA TAAATTTCTT	2880
	AAATCAACTC TTTTTTCTGG TTGTCTGTTT GTTATAAAGT GCAACGKATT CAAGTCCTCA	2940
55	ATATCTGAT CATAATACCA TGCTATAGGA GACTGGGCAA AACCTGTACA ATGACAACCC	3000
	TGGAAGTTGC TTTTTPAAAA AAATAATAAT TTNTTAATCC AAAAAAANA AAAAAANTT	3058

## (2) INFORMATION FOR SEQ ID NO: 95:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1099 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

10 GGCTTTGTAG CTGCTCCGCA GCCCAGCCCG GGCGCGCTCG CAGAGTCCTA GGCGGTGCGC 60  
GGCNTCCGTC CTCTCCCTC CTCGGCGGTC GCGGCCCGCG CCTCCGCGGT GCCTGCCTTC 120  
15 GCTCTCAGGT TGAGGAGCTC AAGCTTGGGA AAATGGTGTG CATTCTTGT ATCGTCATTC 180  
CAGTTCTGCT CTGGATCTAC AAAAAATTCC TGGAGCCATA TATATACCCT CTGGTTTCCC 240  
20 CCTTCGTTAG TCGTATATGG CCTAAGAAAG CAATACAAGA ATCCAATGAT ACAAACAAAG 300  
GCAAAGTAAA CTTTAAGGGT GCAGACATGA ATGGATTACC AACAAAAGGA CCAACAGAAA 360  
TCTGTGATAA AAAGAAAGAC TAAAGAAATT TTCCTAAAGG ACCCCATCAT TTAAAAAATG 420  
25 GACCTGATAA TATGAAGCAT CTTCTTGTG ATTGTCTCTG ACCTTTTAT CTGAGACCGG 480  
AATTCAGGAT AGGAGTCTAG ATATTTACCT GATACTAATC AGGAAATATA TGATATCCGT 540  
ATTTAAAATG TAGTTAGTTA TATTTAATGA CCTCATTCCT AAGTTCCTTT TCGTTAATG 600  
30 TAGCTTTCAT TTCTGTTATT GCTGTTTGAA TAATATGATT AAATAGAAGG TTTGTGCCAG 660  
TAGACATTAT GTTACTAAAT CAGCACTTTA AAATCTTTGG TTCTCTAATT CATATGAATT 720  
35 TGCTGTTGTC TCTAATTCTT TTGGGCTCTT CTAATTTGAG TGGAGTACAA TTTTGTGTG 780  
AAACAGTCCA GTGAACTGT GCAGGGAAAT GAAGGTAGAA TTTTGGGAGG TAATAATGAT 840  
GTGAAACATA AAGATTTAAT AATTACTGTC CAACACAGT GAGCAGCTTG TCCACAAATA 900  
40 TAGTAATTAC TATTTATTGC TCTAAGGAAG ATTAACAAAA GATAGGAAA AGGGGGAAC 960  
TTCTTTGAAA AATGAAACAT CTGTTACATT AATGTCTAAT TATAAAATTT TAATCCTTAC 1020  
45 TGCATTCTT CTGTTCTTAC AAATGTATTA AACATTCAGT TTAACGGTA AAAAAAAAAA 1080  
AAAAAAACCC GGGGGGGG 1099

50

## (2) INFORMATION FOR SEQ ID NO: 96:

## (i) SEQUENCE CHARACTERISTICS:

- 55 (A) LENGTH: 1580 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## 60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

	GGCAGAGACT GGAATCTCTC TTCATGAAAA AATGCAGCCC CTAACTTCA GTTCGACARA	60
5	GTGCAGCTCC TTCTCTCCAC CCACCACAGT GATTCTCCTT ATCCTGCTGT GCTTTGAGGG	120
	CCTGCTCTTC CTCATTTTCA CATCAGTGAT GTTTGGGACC CAGGTGCACT CCATCTGCAC	180
	AGATGAGACG GGAATAGAAC AATTGAAAAA GGAAGAGAGA AGATGGGCTA AAAAAACAAA	240
10	ATGGATGAAC ATGAAAGCCG TTTTGGCCA CCCCTTCTCT CTAGGCTGGG CCAGCCCCTT	300
	TGCCACGCCA GACCAAGGGA AGGCAGACCC GTACCAGTAT GTGGTCTGAA GGACCCCGAC	360
15	CGGCATGGCC ACTCAGACAC AAGTCCACAC CACAGCACTA CCGTCCCATC CGTTCTCATG	420
	AATGTTTAAA TCGAAAAAGC AAAACAATA CTCTTAAAC TTTTMTTATG TCTCAAGTAA	480
	AATGGCTGAG CATTGCAGAG ARAAAAAAAA GTCCCCACAT TTTATTTTTT AAAAACCATC	540
20	CTTTCGATTT CTTTGGTGA CCGAWGCTGC TCTCTTTTCC TTTTAAAATC ACTTCTCTGG	600
	CCTCTGTTTT CTCTCTGCTG TCTGTCTGGC ATGACTAATG TAGAGGGCGC TGTCTCGCGC	660
25	TGTGCCCAT TACTTAATG AGTGAGACAT GACGCTGTGC TGGATGGAAT AGTCTGGACA	720
	CCTGGTGGGG GATGCATGGG AAAGCCAGGA GGGCCCTGAC CTCCCCTGAC CCAGGAGGCA	780
	GTGGCGGGCT CCCCAGTGGG ACATAAAACC TCACCGAAGA TGGATGCTTA CCCCTTGAGG	840
30	CCTGAGAAGG GCAGGATCAG AAGGGACCTT GGCACAGCGA CCTCATCCCC CAAGTGGACA	900
	CGGTTTGCCT GCTAACTCGC AAAGCAATG CCTGCCTTGT ACTTTATGGG CTTGGGGTGT	960
35	GTAAGATGAT TTTGCGGGGG AGTGGGGAGA AAGATGAAAG AGGTCTTATT TGTATCTGA	1020
	ATCAGCAATT ATATTCCCTG TGATTATTTG GAAGAGTGTG TAGGAAAGAC GTTTTCCAG	1080
	TTCAAAATGC CTTATACAAT CAAGAGGAAA AAAAATTACA CAATTTCAAG CAAGCTACGT	1140
40	TTTCCTTGT TTCATCTGCT TCTCTCTCA CCACCCATC TCCCTCTCTT CCCAGCAAG	1200
	ATGTCAATTA AGCAGTGTA ATTCTGACTG CAATAGGCAC CAGTGCCCAA CACATACAGC	1260
45	CCCACCATCA TCCCCTCTC ATTTTATAAA CCTCAAAGTG GATTCACCTT CTGATAGTTA	1320
	ACCCCCATAA ATGTGCACGT ACCTGTGTCT TATCTATATT TTAACCKGGG AGACTGTTGT	1380
	CCTGGGCATG GGAGATGACC ATGATGCTGG GGTACCTCA CAGTCCCCAC CCTTTCAAAG	1440
50	TTNGACATAT GGGCCATCCC ATTGGGCCAG GAATTCCACA GGACACACCT AAGGCTGTGG	1500
	GMAYTGGGGG ACAAATAGAT TTTCCATTTT GAGGAGGGCA CTTTCCCTGT TGTTCAGTTC	1560
55	TTGTTTTGAA GGGAGGTNGG	1580

(2) INFORMATION FOR SEQ ID NO: 97:

60

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 678 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

10 ATATTTTTTTT AGGCTAATGT CCAAGATACA GCATTGAGGA GGCAGCTATG TCTAATGAGG 60  
 GCTCTCTTGT TTGCTAGAGA TGAGAGAAAT GTATACTAAT CATTTTAATT TGTACTTAAA 120  
 ATACATTTTA CTAATCATAT TGATTTTAAA TATGACAAAT TCTTCTAGTA GATACTAATC 180  
 15 TTTCTTGTTT ATCATATTGT CCTAGAGAAG CCTAGGTAAA AATGGGTTCC ACCTAGTCTG 240  
 TTTGTATAAC ACCTTCCCCC GTCCCTCTC CATCCCTGCC AATGGGCTC TATGCATATT 300  
 20 GACAAGCAAA TAAGAAAACC TTAGGTTTCT TGTATTTGAA TTTCCAAAAC AATAAAAGGT 360  
 TTTGACTCAA GATTTGCATT CAAGAAGAGG CAGAAATTTT GTCTTATCTT TTTATCATTT 420  
 TGTGAACTTG TGTTCCTCTG TATGCTTAGA AAATTTTACA CACAAGGAAT GTTTGAAAAA 480  
 25 GTGAGAATTT TAGAGTGCTT GGGTGGTTT TATTGGTCA GTGCTGATGT GTTARGTGTT 540  
 TAGGGAAATA ATGCTTCAGG ACCTTTTGA CAACACAGYT TCATGAATGA CYGGGGGATA 600  
 30 TTWAKGTTGT GCTGAGAAAA GGGAGGGAGT GGGCAGTTGG AATGGGGGAC CCTTACCATT 660  
 GGAAAACATG CATTCTNGN 678

35

## (2) INFORMATION FOR SEQ ID NO: 98:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1253 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

40

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

45

ACCTCCCTCC CTCTCAGACT GGTCCGAATC CACGCCTAGC CCAGCCACTG CCACTGGGGC 60  
 CATGGCCACC ACCACTGGGG CACTGCCTGC CCAGCCACTT CCCTTGCTCTG TTCCCAGCTC 120  
 50 CCTTGCTCAG GCCCAGACCC AGCTGGGGCC CCACCGNAA GTTACCCCCA AGAGGCAAGT 180  
 NITGGCCTGA GACGCTCGTC AGTTCTTAGA TCTTGGGGGC CTAAAGAGAC CCCCCTCCTG 240  
 55 CCTCCTTCTT TTCTCTGTCT CTTCCTTCCT TTTAGTCTTT TTCATCCTCT TCTCTTTCCA 300  
 CCAACCCTCC TGCATCCTTG CCTTGCAGCG TGACCGAGAT AGGTCATCAG CCCAGGGCTT 360  
 CAGTCTTCCT TTATTTATAA TGGGTGGGGG CTACCACCCA CCCTGCTGCA GTCTTGTA 420  
 60 GAGTCTGGGA CCTCCTTCTT CCCCACTTCT CTCTTCCTC ATTCTTCTCT CTCTCCTTCT 480

5 GGCTCTCAT TTCCTTACAC TCTGACATGA ATGAATTATT ATTATTTTTTC TTTTTCTTTT 540  
 TTTTTTTTACA TTTTGTATAG AAACAAATTC ATTTAAACAA ACTTATTATT ATTATTTTTT 600  
 ACAAATATA TATATGGAGA TGCTCCCTCC CCCTGTGAAC CCCCCAGTGC CCCCCTGGGC 660  
 TGNAGTCTGT GGGCCCATTC GGCCAAGCTG GATTCTGTGT ACCTAGTACA CAGGCATGAC 720  
 10 TGGGATCCCG TGTACCGAGT ACACGACCCA GGTATGTACC AAGTAGGCAC CCTTGGGCGC 780  
 ACCCACTGGG GCCAGGGGTC GGGGAGTGT TGGGAGCCTC CTCCCCACCC CACCTCCCTC 840  
 ACTTCACTGC ATTCCAGATT GGACATGTTT CATAGCCTTG CTGGGGAAGG GCCCACTGCC 900  
 15 AACTCCCTCT GCCCCAGCCC CACCCTTGGC CATCTCCCTT TGGGAAGTAG GGGGCTGCTG 960  
 GTGGGAAATG GGAGCCAGGG CAGATGTATG CATTCCTTTA TGTCCCTGTA AATGTGGGAC 1020  
 20 TACAAGAAGA GGAGCTGCCT GAGTGGTACT TTCTCTTCCT GGTAATCCTC TGGCCCAGCC 1080  
 TTATGGCAGA ATAGAGGTAT TTTTAGGCTA TTTTGTAAAT ATGGCTTCTG GTCAAAATCC 1140  
 CTGTGTAGCT GAATTCCTCA GGCCTGCATT GTACAGCCCC CCACTCCCTT CACCACCTAA 1200  
 25 TAAAGGAATA GTTAACACTC AAAAAAAAAA AAAAAAAAAA ACTTGAGGGG GGG 1253

30

(2) INFORMATION FOR SEQ ID NO: 99:

(i) SEQUENCE CHARACTERISTICS:

35

- (A) LENGTH: 447 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

40

CAAAGAATGA AATTTACCAC TCTCCTCTTC TTGGCAGCTG TAGCAGGGGC CCTGGTCTAT 60  
 GCTGAAGATG CCTCCTCTGA CTCGACGGGT GCTGATCCTG CCCAGGAAGC TGGGACCTCT 120  
 45 AAGCCTAATG AAGAGATCTC AGGTCCAGCA GAACCAGCTT CACCCCCAGA GACAACCACA 180  
 ACAGCCCAGG AGAYTTCGGC GGCAGCAGTT CAGGGGACAG CCAAGGTCAC CTCAAGCAGG 240  
 CAGGAACTAA ACCCCCTGAA ATCCATAGTG GAGAAAAGTA TCTTACTAAC AGAACAAGCC 300  
 50 CTTGCAAAAG CAGGAAAAGG AATGCACGGA GCGTGCCAG GTGGAAAACA ATTCATCGAA 360  
 AATGGAAGTG AATTGACACA AAAATTACTG AAGAAATTCA CTCTATTAAA ACCATGGGCA 420  
 55 TGAGAAGCTG AAAAGAATKG GATCATT 447

60

(2) INFORMATION FOR SEQ ID NO: 100:



## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 611 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

10 GGTCTGGGGA GGTGACATGT TGGGCTGTGG GATCCAGCG CTGGGCCTGC TCCTGCTGCT 60  
GCAGGSWTCG GCAGACGGAA ATGGAATCCA GGGATTCTTC TACCCATGGA GCTGTGAGGG 120  
TGACATATGG GACCGGGAGA GCTGTGGGGG CCAGGCGGCC ATTCGATAGC CCCAACYTCT 180  
15 GCCTGCGTCT CCGGTGCTGC TACCGCAATG GGTCTGCTAC CACCAGCGTC CAGACGAAAA 240  
CGTGCGGAGG AAGCACATGT GGGCGCTGGT CTGGACGTGC AGCGGCCTCC TCCTCCTGAG 300  
20 CTGCAGCATC TGCTTGTTMT GGTGGGCCAA GCGCCGGGAC GTGCTGCATA TGCCCGGTTT 360  
CCTGGCGGGT CCGTGTGACA TGTCCAAGTC CGTCTCGCTG CTCTCCAAGC ACCGAGGGAC 420  
CAAGAAGACG CCGTCCACGG GCAGCGTGCC AGTCGCCCTG TCCAAAGAGT CCAGGGATGT 480  
25 GGAGGGAGGC ACCGAGGGGG AAGGGACGGA GGAGGGTGAG GAGACAGAGG GCGAGGAAGA 540  
GGAGGATTAG GGGAGTCCCC GGGGGACTGG TCAATACAGA TACGGTGGAC GGAAAAAAAA 600  
30 AAAAAAAAAA A 611

## 35 (2) INFORMATION FOR SEQ ID NO: 101:

## (i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 609 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

45 GCATTGGTAA AGCTGGCAGT TGAACCAGT TGGACGGCCC AGCTTGCGTC TCTTCTGCCT 60  
GAGTGGGCCT CTCAGGTCAC TCGTGCCCTG CTGGAGGACA GAGGGGCACC TCAGCCGCCC 120  
CCAAGCCCAG AGCACAGCAA TAAGTCGGC CTGCAGGAGC CGGGGTGGGG GTGGGGGTGG 180  
50 GGGGRGCAGG ACCCTRARAT GCCACCAGGA CCTGATGGGC CAGGAAGGGC GTGGACATGG 240  
AGGCTGTTTT TACAGTTTTT TTTTTTTTGT TTTTTTGT TTAAAGAATA CAGAAGGAGC 300  
55 CAAGCTTTTT TGCACTTTGT ATCCAGCTGC AAGCTCAAGG CAGAGTCAAG GGCTTGGGTT 360  
GGAAAAACCT GACTCACAGG AATGCATAAT TGACCTTGC AGCTACCCAA TAGCCCTTGG 420  
AGCTGGCACT GAACCAGGCT GCAAGATTG ACTGCCTTAA AAACACAAGG CCTCTAGGC 480  
60

CTGGCAGGGA TGTCCTGTG CCCAGCACTG GGGGCTCGAA GACTGGTTTC TAGCACTACC 540  
 GGTCACGGCC ATGTCGTCTT AGAAGGGTCC AGAAGATTAT TTTACGTTGA GTCCATTTTT 600  
 5 AATGTTCTG 609

10 (2) INFORMATION FOR SEQ ID NO: 102:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 1770 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

20 ACGGYCCGGA ATCCCGGGTG GACCCACGCG TCCGGGAAAT TGAAACTGAG TGGCCACGA 60  
 TGGGAAGAGG GGAAAGCCCA GGGGTACAGG AGGCCTCTGG GTGAAGGCAG AGGCTAACAT 120  
 25 GGGGTTCGGA GCGACCTTGG CCGTTGGCCT GACCATCTTT GTGCTGTCTG TCGTCACTAT 180  
 CATCATCTGC TTCACCTGCT CTGTCTGTCT CCTTTACAAG ACGTGCCGCC GACCACGTCC 240  
 GGTGTGCACC ACCACCACAT CCACCACTGT GTGTCATGCC CCTTATCCTC AGCCTCCAAG 300  
 30 TGTGCCGCCC AGCTACCCTG GACCAAGCTA CCAGGGCTAC CACACCATGC CGCCTCAGCC 360  
 AGGGATGCCA GCAGCACCTT ACCCAATGCA GTACCCACCA CCTTACCCAG CCCAGCCCCAT 420  
 35 GGGCCACCG GCCTACCACG AGACCCTGGC TGGAGGAGCA GCGCGCCCT ACCCCGCCAG 480  
 CCAGCCTCCT TACAACCCGG SCTACATGGA TGCCCCGAAG SGGNCCTCTG AGCATTCCTT 540  
 GGCCTCTYTG GCTGCCACTT GGTATGTGTG TGTGTGTGCG TGARTGGTGT GCAGGCGCGG 600  
 40 TTCCTTACGC CCCATGTGTG CTGTGTGTGT CCTGCCTGTA TATGTGGCTT CCTCTGATGC 660  
 TGACAAGGTG GGGAAACAAT CTTGCCAGAG TGGGCTGGGA CCAGACTTTG TTCTCTTCTT 720  
 CACCTGAAAT TATGCTTCCT AAAATCTCAA GCCAACTCA AAGAATGGGG TGGTGGGGGG 780  
 45 CACCCTGTGA GGTGGCCCCCT GAGAGGTGGG GGCCTCTCCA GGGCACATCT GGAGTTCTTC 840  
 TCCAGCTTAC CCTAGGGTGA CCAAGTAGGG CTGTACAC CAGGGTGGCG CAGCTTTCTG 900  
 50 TGTGATGCAG ATGTGTCCTG GTTTCGGCAG CGTAGCCAGC TGCTGCTTGA GGCCATGGCT 960  
 CGTCCCCGGA GTTGGGGGTA CCCGTTGCAG AGCCAGGGAC ATGATGCAGG CGAAGCTTGG 1020  
 55 GATCTGGCCA AGTTGGACTT TGATCTTTTG GGCAGATGTC CCATTGCTCC CTGGAGCCTG 1080  
 TCATGCCTGT TGGGATCAG GCAGCCTCCT GATGCCAGAA CACCTCAGGC AGAGCCCTAC 1140  
 TCAGCTGTAC CTGTCTGCCT GGAAGTGTCC CTGTCCCCGC ATCTCCCCCT GGACCAGCTG 1200  
 60 GAGGGCCACA TGCACACACA GCCTAGCTGC CCCCAGGGAG CTCTGCTGCC CTTGCTGGCC 1260

CTGCCCTTCC CACAGGTGAG CAGGGCTCCT GTCCACCAGC ACACTCAGTT CTCTTCCCTG 1320  
 CAGTGTTCATC ATTTTATTTT AGCCAAACAT TTGCTCTGTT TTCTGTTTCA AACATGATAG 1380  
 5 TTGATATGAG ACTGAAACCC CTGGGTGTGT GAGGGAAATT GGCTCAGAGA TGGACAACCT 1440  
 GGCAACTGTG AGTCCCTGCT TCCCGACACC AGCCTCATGG AATATGCAAC AACTCCTGTA 1500  
 10 CCCAGTCCA CGGTGTTCTG GCAGCAGGA CACCTGGGCC AATGGGCCAT CTGGACCAA 1560  
 GGTGGGTGT GGGGCCCTGG ATGGCAGCTC TGGCCAGAC ATGAATACCT CGTGTTCCTC 1620  
 CTCCCTCTAT TACTGTTTCA CCAGAGCTGT CTTAGCTCAA ATCTGTTGTG TTTCTGAGTC 1680  
 15 TAGGTCTGT AACTTGTTC ATAATAAATG CAATCGTTTG GAAAAAATAA AAAAAAATAA 1740  
 TCGTAGGGGG GGGCGTACC CAATSGCCTA 1770  
 20

## (2) INFORMATION FOR SEQ ID NO: 103:

- 25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1832 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear  
 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

TGTGGCTGAC GTCATCTGGA GGAGATTGTC TTTCTTTTTC TCCAAAAGGG GAGGAAATTG 60  
 35 AAATGTCAGT GGGCCACGAT GGAAGAGGG GAAAGCCCAG GGTACAGGA GGCCTCTGGG 120  
 TGAAGGCAGA GGCTAACATG GGTTCGGAG CGACCTTGGC CGTTGGCTGA CCATCTTTGT 180  
 GCTGTCTGTC GTCACATCA TCATCTGCTT CACCTGCTCC TGCTGCTGCC TTTACAAGAC 240  
 40 GTGCGCCGA CCACGTCCGG TTGTACCCAC CACCACATCC ACCACTGTGG TGCATGCCCC 300  
 TTATCCTCAG CCTCCAAGTG TGCCGCCAG CTACCCTGGA CCAAGCTACC AGGGCTACCA 360  
 45 CACCATGCCG CTCAGCCAG GGATGCCAGC AGCACCCTAC CCAATGCAGT ACCCACCACC 420  
 TTACCCAGCC CAGCCCATGG GCCCACCAGC CTACCACGAG ACCCTGGCTG GAGGAGCAGC 480  
 CGCGCCCTAM CCCGSCAGCC AGCCTCCTTA CAACCCGGCC TACATGGATG CCCGAAGCGG 540  
 50 CCCTCTGAGC ATTCCCTGGC CTCTYTGCT GCCACTTGGT TATGTTGTGT GTGTGCGTRA 600  
 GTGGTCTGCA GCGCGGTTTC CTTACGCCCC ATGTGTGCTG TGTGTGTCCA GGCACGGTTC 660  
 55 CTTACGCCCC ATGTGTGCTG TGTGTGCTT GCCTGTATAT GTGGTTTCCT CTGATGCTGA 720  
 CAAGTGGGGA ACAATCCTTG CCAGAGTGGG CTGGGACCAG ACTTTGTTCT CTTCTCACC 780  
 60 TGAAATTATG CTTCTTAAAA TCTCAAGCCA AACTCAAAGA ATGGGGTGGT GGGGGGCACC 840

	CTGTGAGGTG GCCCTGAGA GGTGGGGGCC TCTCCAGGCG ACATCTGGAG TTCTTCTCCA	900
	GCTTACCCTA GGGTGACCAA GTAGGGCCTG TCACACCAGG GTGGCGCAST TTCTGTGTGA	960
5	TGCAGATGTG TCCTGGTTTC GGCAGCGTAG CCAGCTGCTG CTTGAGGCCA TGGCTCGTCC	1020
	CCGGAGTTGG GGGTACCCGT TGCAGAGCCA GGGACATGAT GCAGGCGAAG YTTGGGATCT	1080
10	GGCCAAGTTG GACTTTGATC CTTTGGGCAG ATGTCCCATF GCTCCCTGGA GCCTGTCATG	1140
	CCTGTTGGGG ATCAGGCAGC CTCCTGATGC CAGAACACCT CAGGCAGAGC CCTACTCAGC	1200
	TGTACCTGTC TGCCTGGACT GTCCCCTGTC CCCGCATCTC CCCTGGGACC AGCTGGAGGG	1260
15	CCACATGCAC ACACAGCCTA GCTGCCCCCA GGGAGCTCTG CTGCCCTTGC TGGCCCTGCC	1320
	CTTCCCACAG GTGAGCAGGG CTCCTGTCCA CCAGCACACT CAGTTCTCTT CCCTGCAGTG	1380
20	TTTTCATTTT ATTTTAGCCA AACATTTTGC CTGTTTTCTG TTTCAAACAT GATAGTTGAT	1440
	ATGAGACTGA AACCCCTGGG TTGTGGAGGG AAATTGGCTC AGAGATGGAC AACCTGGCAA	1500
	CTGTGAGTCC CTGCTTCCCG ACACCAGCCT CATGGAATAT GCAACAACCT CTGTACCCCA	1560
25	GTCCACGGTG TTCTGGCAGC AGGGACACCT GGGCCAATGG GCCATCTGGA CCAAAGGTGG	1620
	GGTGTGGGGC CCTGGATGGC AGCTCTGGCC CAGACATGAA TACCTCGTGT TCCTCCTCCC	1680
30	TCTATTACTG TTTCACCAGA GCTGTCTTAG CTCAAATCTG TTGTGTTTCT GAGTCTAGGG	1740
	TCTGTACACT TGTTTATAAT AAATGCAATC GTTTNGGAAA AAAAAANANAA AAAAAAAGG	1800
	GGSGGCGCTC TAAAAGGATN CCCNAAGGG GG	1832
35		

## (2) INFORMATION FOR SEQ ID NO: 104:

- 40 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 2237 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: linear
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

	AGTTCCCGGT ACTTTATTAC CAAGGTGACC ATCGGAACCA GGAATGACAT TACTCACTAT	60
50	CAGAATTGAG AAAATTGGTT TGAAAGATGC TGGGCAGTGC ATCGATCCCT ATATTACAGT	120
	TAGTGTAAG GATCTGAATG GCATAGACTT AACTCCTGTG CAAGATACTC CTGTGGCTTC	180
55	AAGAAAAGAA GATACATATG TTCATTTTAA TGTGGACATT GAGCTCCAGA AGCATGTTGA	240
	AAAATTAACC AAAGGTGCAG CTATCTTCTT TGAATTCAAA CACTACAAGC CTAAAAAAG	300
	GTTTACCAGC ACCAAGTGTG TTGCTTTCAT GGAGATGGAT GAAATTAAAC CTGGGCCAAT	360
60	TGTAATAGAA CTATACAAGA AACCCACTGA CTTTAAAAGA AAGAAATTGC AATTATTGAC	420

	CAAGAAACCA CTTTATCTTC ATCTACATCA AACTTTGCAC AAGGAATGAT CCTGACATGA	480
5	TGAACCTGGA ACTTCTGTGA ATTTTACCAC TCAGTAGAAA CCATCATAGC TCTGTGTAGC	540
	ATATTCACCC TTCAACAGGC AGGAAGCAAG CCGTACCCAG ACCAGTAGGC CGGACGGAGT	600
	CAATNGCAAA GCTGTACCAC AGAATTCAGA GTCCAGCACA TCACACTGAC GTATAGGACT	660
10	CCTTGGGATA CAGGTTTATT GTAGATTTTG AAACATGTTT TTAATTTTCT ATTAATTTGTG	720
	CAATTAATAG TCTATTTTCT AATTTACCAC TACTCCTACC CTGCTTCCTG GAACAATACT	780
15	GTTGTGGGTA GGATGTGCTC ATCTTCAGAC TTAATACAGC AATAAGAATG TGCTAGAGTT	840
	TACACATCTG TTCACTTTGT CTCCAATATG CTCCTTTGAC TTAACGTCAA GCTTTGGGTT	900
	GATGTGGGTA GGGTAGTGTC AAAGTGTCTT GAGAGGAATG GGACCAGTTC TGCTGCCTAA	960
20	GAAGGTCTGT CTGGATGTTT ATAGGCAGCA CCTCTGAAGT GGCCTAAATT CACCCTGATC	1020
	TGATAGTTTT CTGCTTAGA AAGTGTGCCT TGGCCAGATC AGTATCCAC ATGGGAGTGT	1080
25	TCCCTAGGTT GTAGCTGTGA TTGTTTCCAG ATGACCAGAT TGTTTTCTG AAAATGAGCA	1140
	TATTTTGTAGT CATGTCGATT AGCTGTTCTT CTACATCACA TTGTTACTCT TTCTGATGAT	1200
	GATTCTAGGG TTAACATGG AACCATCTCA AAATAATTAC AAAGTTTATG ATGGGTTTAC	1260
30	AATGTCTTCT AAACAATGTA ATCTAAAAAT AATTGAGTCA GATGCTAACG AGATACTGCA	1320
	GGCATAACTG CTGTTTCTCT GACAACCTGAT TGTGAAACCT TAAACCTGC ATACCTCTTC	1380
35	TTACAGTGAG GAGTATGCAA AATCTGGAAA GATATTCTAT TTTTTTTATA TAGGTAGATA	1440
	GGATCGCCAT TTATTTCTTA TTAGATATA CTGACATTCA TCCATATGAA AATATGCAGG	1500
	TCATTAGCTT ACTATAATTT ACTTTTGAAT TAATGGGGCA TAAATAAAAC TTTCATAGTA	1560
40	CACATGAGGT GGATATTGA TACACAGAAC ATTTGCGGTG GGCTTTCTGT GGGTTAGATG	1620
	TAAAGCCAC ATATTTTAAT ATTCATAAT TTAAATGAGC AATGCATGAG GGAATGCAG	1680
45	TGTCAGTACC TGGCCTATTT TTAACTAGT GTAATCACC TAGTCATACC ATTCAGTATG	1740
	TTTGCTTTTT AAAATAAGTA ACCACAATTA AGTTGTGTGA GCCCTTGCAC TTCAAGAGAT	1800
	CTAGTCTTTA CTTTCAGTTG TCTGTTAGGT CCATTCGTGT TACTAGACGG ATGTTAATAA	1860
50	AAACTATGCG AGCCTGAATG AATTCTCAGC CAAATTTAGT CTTGTCTCTC ATCTTGATTG	1920
	GATTAATTCC AAATTCTAAA ATGATTCACT CCACAATAGC TCTAGGGGAT GAAGAATTTG	1980
55	CCTTACTTTG CCCAGTTTCT AAGACTGTGA GTTGTCAAAT CCCTAGACTG TAAGCTCTTC	2040
	AAGGAGCAAG AGGCGCATTT TCTCCGTGTC ATGTAATTTT TCTAAGGTGT TTGGCAGCAC	2100
	TCTGTACCCT GTGGAGTACT CAGTACCTTT TGTTTGATGT TGCTGACAAG ACCTGAAAAA	2160
60	AAATCCCTTA AAAAAAAAC CCATTAAAGT GTAGCAAAAC CGAAAAAAA AAAANAAAAA	2220

ACTCGAGACG GGCCCCG

2237

5

(2) INFORMATION FOR SEQ ID NO: 105:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1822 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

	GGTCGACCCA CGCGTCCGGA ATTTTCGTAG CAATAAGTTT GTGCATGTAT AGTAATTTGC	60
	ATTAGCAAGG TTGTAACCTC TGCCTCTTGG GTTCAAGTGA TTCTCGTGCC CCAGCCTCCC	120
20	GAGTAGCTGG GACTACAGGC ACGTGCCACC ACGCCAGCT AATTTTTATA TTTTATAGTAG	180
	AGACGGGGTT TTGCTGTGTT GGCCAGGCTG GTCTCAAACT CCTGACCTCA AGTAATCCAC	240
25	CTGGCCTGCT CTTTTCATGT CTTAACATGG CATGCTTTT AGTTTCATTA TTTTCCTACT	300
	CCTTGTATGT CAAGAAATTA CATTTTGCAT GTCTTATGGA GATGCTGTGA ATTGCTTCAG	360
	TGAGTGCTTT TCTAATCTGC AGACCATTTA CATTCCTGT TTGCAGCATG CTGTGTGCAA	420
30	ACACTCAGTA ATTTGGAGTA TTCAATTATT TGTTAGGGCT CTTCTATTT CCAAATGTGC	480
	TGAATGTCT ATTGATGGA TTTTCAGATC TTTTCATGAG AACTGGAAAT GTAGCTGGGT	540
35	GGCACCTACC TAGGTGCTA CGTAGTGAGT AGACTTTCTC TTGGGTATAG TAAGCCTCAG	600
	ACAGCTTTCA CTTTATCTA CTTTACTTGT GGAAATAAAA CAGTCATTTT GTTCTGAAAG	660
	AATAAGATAG CTTTCTGTAG AGAAGGAATT CCTACCTCTA AAAGCTGCCT TGAGAACTCA	720
40	GAAGTGGCAG TTTTCTGAGG TGATTTTAA ATTTTCAGTAT TAGGGAGAGT CCAGCATTTG	780
	CTGACACAGA TTCTACATAA CTAATGTATG ATAGCAAATG CAAACTATT ATAATGTGGT	840
45	GTATCTTGGC CATACACAGG TTAGAACAAG TAGACTCTGG CAGCAGATCT CCAGAGACCC	900
	AAGTTTAGGT TCTCATAGT TATTTGAAGT AGTTATACTC CTGGCTTAAG TAGTTTAGTG	960
	CCTGGGAGAA TCCATTACTG AAAAGCATTT AACTTAAAAA AAAAAAAAAA AAAAAAAAAA	1020
50	AAACCTCGTG CGAATTCCG CACGAGCTAA CCCAGAAACA TCCAATTCTC AACTGAAGC	1080
	TGCACTCTC GCCTCCAGCA TGAAAGTCTC TGCCGCCCTT CTGTGCCTGC TGCTCATAGC	1140
55	AGCCACCTTC ATTCCTCAAG GGCTCGCTCA GCCAGATGCA ATCAATGCCC CAGTCACCTG	1200
	CTGYTATAAC TTCACCAATA GGAAGATCTC AGTGCAGAGG CTCGCGAGCT ATAGAAGAAT	1260
60	CACCAGCAGC AAGTGTCCCA AAGAAGCTGT GATCTTCAAG ACCATTGTGG CCAAGGAGAT	1320

CTGTGCTGAC CCCAAGCAGA AGTGGGTTCA GGATTCATG GACCACCTGG ACAAGCAAAC 1380  
 CCAAACCTCG AAGACTTGAA CACTCACTCC ACAACCCAAG AATCTGCAGC TAACTTATTT 1440  
 5 TCCCCTAGCT TTCCCCAGAC ACCCTGTTTT ATTTTATTAT AATGAATTTT GTTGTGTGAT 1500  
 GTGAAACATT ATGCCTTAAG TAATGTAAAT TCTTATTTAA GTTATGATG TTTTAAGTTT 1560  
 10 ATCTTTTCATG GTACTAGTGT TTTTGTAGATA CAGAGACTTG GGGAAATTGC TTTTCTCTT 1620  
 GAACCACAGT TCTACCCCTG GGATGTTTTG AGGGTCTTTG CAAGAATCAT TAATACAAAG 1680  
 AATTTTTTTT AACATTCCAA TGCATTGCTA AAATATTATT GTGGAAATGA ATATTTTGTA 1740  
 15 ACTATTACAC CAAATAAATA TATTTTGTGA CAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 1800  
 AAGSGGCCGC TCGAATTAAG CC 1822

20

(2) INFORMATION FOR SEQ ID NO: 106:

25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1712 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

CGTGCCCCAG CCTCCCGAGT AGCTGGRAC ACAGGCACGT SCCACCACGC CCAGCTAATT 60  
 TTWATATTTT WAGTAGAGAC GGGGTTTTSC TGTRTTGGCC AGGCTGGTCT CAAACTCCTG 120  
 35 ACCTCAAGTA ATCCACCTGG CCTGCTCTTT TCATGTCTTA ACATGGCATG TCTTTTAGTT 180  
 TCATTATTTT CCTACTCCTT GTATGTCAAG AAATTACATT TTGCATGTCT TATGGAGATG 240  
 40 CTGTTAATTG CTTCACTGAG TGCTTTTCTA ATCTGCAGAC CATTTACATT TCCTGTTTGC 300  
 AGCATGCTGT GTGCAAACAC TCAGTAATTT GGAGTATTCA ATTATTTGTT AGGGCTCTTC 360  
 CTATTTCCAA ATGTGCTGAA TTGTCTATTG ATGGGATTTT CAGATCTTTT CATGAGAACT 420  
 45 GGAAATGTAG CTGGGTGGCA CCTACCTAGG TTGCTACGTA GTGAGTAGAC TTTCTCTTGG 480  
 GTATAGTAAG CCTCAGACAG CTTTCACTTT TATCTACTTT ACTTGTGGAA ATAAACAGT 540  
 50 CATTTTGTTC TGAAAGAATA AGATAGCTTT CTGTAGAGAA GGAATTCCTA CCTCTAAAAG 600  
 CTGCCTTGAG AACTCAGAAC TGGCAGTTTT CTGAGGTGAT TTTTAAATTT CAGTATTAGG 660  
 GAGAGTCCAG CATTTGCTGA CACAGATTCT ACATACTAA TGTATGATG CAAATGCAAA 720  
 55 ACTATTATAA TGTGGTGTAT CTTGCGCATA CACAGTTAG AACAAAGTGA CTCTGGCAGC 780  
 AGATCTCCAG AGACCCAAGT TTAGGTCTCT ATAGTGATT TGAAGTAGTT ATACTCCTGG 840  
 60 CTTAAGTAGT TTAGTGCTG GGAGAATCCA TTAAGTAAAA GCATTTAACT TAAAAAAAAA 900

	AAAAAAAAA AAAAAAAAAAC CTCGTGCCGA ATTCGGCACG AGCAGAAACA TCCAATTCTC	960
5	AAACTGAAGC TCGCACTCTC GCCTCCAGCA TGAAAGTCTC TGCCGCCCTT CTGTGCCTGC	1020
	TGCTCATAGC AGCCACCTTC ATTCCCAAG GGCTCGCTCA GCCAGATGCA ATCAATGCCC	1080
	CAGTCACCTG CTGYTATAAC TTCACCAATA GGAAGATCTC AGTGCAGAGG CTCGCGAGCT	1140
10	ATAGAAGAAT CACCAGCAGC AAGTGTCCTA AAGAAGCTGT GATCTTCAAG ACCATTGTGG	1200
	CCAAGGAGAT CTGTGCTGAC CCCAAGCAGA AGTGGGTTCA GGATTCCATG GACCACCTGG	1260
15	ACAAGCAAAC CCAAACCTCG AAGACTTGAA CACTCACTCC ACAACCCAAG AATCTGCAGC	1320
	TAACCTATTT TCCCTAGCT TTCCCAGAC ACCCTGTTTT ATTTTATTAT AATGAATTTT	1380
	GTTTGTGAT GTGAAACATT ATGCCTTAAG TAATGTTAAT TCTTATTAA GTTATTGATG	1440
20	TTTTAAGTTT ATCTTTCATG GTACTAGTGT TTTTGTAGATA CAGAGACTTG GGGAAATTGC	1500
	TTTTCCTCTT GAACCACAGT TCTACCCCTG GGATGTTTTG AGGGTCTTTG CAAGAATCAT	1560
25	TAATACAAAG AATTTTTTTT AACATTCCAA TGCATGCTA AAATATTATT GTGGAATGA	1620
	ATATTTTGTA ACTATTACAC CAAATAAATA TATTTTGTGA CAAAAAAAAA AAAAAAAAAA	1680
30	AAAAAAAAA AAGSGGCCGC TCGAATTAAG CC	1712

## (2) INFORMATION FOR SEQ ID NO: 107:

- 35 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1969 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: linear
- 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

	CCCCTCCTTC CCCTYGCCAC CTACTGAACC CTCCTCGAG GTGCCCGAGC AGCCGTCTGC	60
45	CCAGCCACTC CCTGGGAGTC CCCCAGAAG AGCCTATTAC ATCTACTCCG GGGGCGAGAA	120
	GATCCCCCTG GTGTGAGCC GGCCCTCTC CTCCAACGTG GCCACTCTTC AGCATCTCTG	180
50	TCGGAAGACC GTCAACGGCC ACCTGGACTC CTATGAGAAA GTCACCCAGC TGCCGGGGCC	240
	CATTGGRAG TTCCTGGACC AGTACGATGC CCCGTTTTAA GGGGTAAAGG GCGCAAAGGG	300
	CATGGGTCCG GAGAGGGGAC GCAGGCCCT CTCCTCGTG GCACATGGCA CAAGCACAG	360
55	AAGCCAACCA GGAGAGATC CTGTAGCTCT GGGGGGAAAG AGGGCCGACA CCCCCCTCC	420
	TCTGCCCTCT CCCTGCAGAA TGTGGCAGGC GGACCTGGAA TGTGTTGGAG GGAAGGGGA	480
60	GTACCACCTG AGTCTCCAGC TTCTCCGGAG ACCCAGCTGT CCTGGTGGGA CGATAGCAAC	540



CACAAGTGGA TTCTCCTTCA ATTCTCAGC TTCCCTCTG CCTCCAAACA GGGGACACTT 600  
 CGGGAATGCT GAAYTAATGA GAACTGCCAG GGAATCTTCA AACTTTCCAA CGGAACCTGT 660  
 5 TTGCTCTTTG ATTTGGTTTA AACCTGAGCT GGTGTGGAG CCTGGGAAAG GTGGAAGAGA 720  
 GAGAGGTCCT GAGGGCCCCA GGGSTGCGGG CTGGCGAAGG AAATGGTCAC ACCCCCCGCC 780  
 10 CACCCCAGGC GAGGATCCTG GTGACATGCT CCTCTCCCTG GCTCCGGGGA GAAGGGCTTG 840  
 GGGTGACCTG AAGGGAACCA TCCTGGTGCC CCACATCCTC TCCTCCGGN ACAGTCACCG 900  
 AAAACACAGG TTCCAAAGTC TACCTGGTGC CTGAGAGCCC AGGGCCCTTC CTCCGTTTAA 960  
 15 AGGGGGAAGC AACATTTGGA GGGGACGGAT GGGCTGGTCA GCTGGTCTCC TTTTCCTACT 1020  
 CATACTATAC CTTCTGTAC CTGGGTGGAT GGAGCGGAG GATGGAGGAG ACGGGACATC 1080  
 TTTCACCTCA GGCTCCTGGT AGAGAAGACA GGGGATTTCTA CTCTGTGCCT CTGACTATG 1140  
 20 TCTGGCTAAG AGATTGCGCT TAAATGCTCC CTGTCCCATG GAGAGGGACC CAGCATAGGA 1200  
 AAGCCACATA CTCAGCCTGG ATGGGTGGAG AGGCTGAGGG ACTCACTGGA GGGCACCAAG 1260  
 25 CCAGCCCACA GCCAGGGAAG TGGGGAGGGG GGGCGGAAAC CCATGCCTCC CAGCTGAGCA 1320  
 CTGGGAATGT CAGCCCAGTA AGTATTGCC AGTCAGGCGC CTCGTGGTCA GAGCAGAGCC 1380  
 ACCAGGTCCC ACTGCCCCGA GCCCTGCACA GCCCTCCCTC CTGCCTGGGT GGGGGAGGCT 1440  
 30 GGAGGTCATT GGAGAGGCTG GACTGCTGCC ACCCCGGGTG CTCCCGCTCT GCCATAGCAC 1500  
 TGATCAGTGA CAATTTACAG GAATGTAGCA GCGATGGAAT TACCTGGAAC ATTTTTTGT 1560  
 35 TTTGTTTTTG TTTTGT TGTGGGGGG GCAACTAAA CAAACACAAA GTATTCTGTG 1620  
 TCAGGTATTG GGCTGGACAG GGCAGTTGTG TGTGGGGTG GTTTTTTCT CTATTTTTTT 1680  
 GTTGTCTCT TGTTTTTTAA TAATGTTTAC AATCTGCCTC AATCACTCTG TCTTTTATAA 1740  
 40 AGATTCCACC TCCAGTCTC TCTCTCCCC CTTACTCAGG CCCTTGAGGC TATTAGGAGA 1800  
 TGCTTGAAGA ACTCAACAAA ATCCCAATCC AAGTCAAAC TTGCACATAT TTATATTTAT 1860  
 45 ATTGAGAAAA GAAACATTTC AGTAATTTAT AATAAGAGC ACTATTTTTT AATGAAAAAA 1920  
 AAAAAAAAAA AAAAAAAAAA CGACGCTGGT GACCGGAATY CGACGTACG 1969

50

(2) INFORMATION FOR SEQ ID NO: 108:

55

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1734 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

	CGGGTCCCAA GCCTGTGCCT GAGCCTGAGC CTGAGCCTGA GCGCGAGCCG GGAGCCGGTC	60
5	GCGGGGGCTC CGGGCTGTGG GACCGCTGGG CCCCCAGCGA TGGCGACCCT GTGGGGAGGC	120
	CTTCTTCGGC TTGGCTCCTT GCTCAGCCTG TCGTGCCTGG CGCTTTCCGT GCTGCTGCTG	180
	GCGCATGTNC AGACGCCGCC AAGAATTTTCG AGGATGTCAG ATGTAAATGT ATCTGCCCTC	240
10	CCTATAAAGA AAATTCGTGG CATATTTATA ATAAGACAT ATCTCAGAAA GATTGTGATT	300
	GCCTTCATGT TGTGGAGCCC ATGCCTGTGC GGGGGCCTGA TGTAGAAGCA TACTGTCTAC	360
15	GCTGTGAATG CAAATATGAA GAAAGAAGCT CTGTCACAAT CAAGGTACC ATTATAATTT	420
	ATCTCTCCAT TTTGGGCCTT CTACTTCTGT ACATGGTATA TCTTACTCTG GTTGAGCCCA	480
	TACTGAAGAG GCGCCTCTTT GGACATGCAC AGTTGATACA GAGTGATGAT GATATTGGGG	540
20	ATCACCAGCC TTTTGCAAAT GCACACGATG TGCTAGCCCG CTCCCGCAGT CGAGCCAACG	600
	TGCTGAACAA GGTAGAATAT GCACAGCAGC GCTGGAAGCT TCAAGTCCAA GAGCAGCGAA	660
25	AGTCGTCTTT TGACCGGCAT GTTGTCTCTA GCTAATTGGG GAATTGAATT CAAGGTGACT	720
	AGAAAGAAAC AGGCAGACAA CTGGGAAAGA ACTGACTGGG NTTTTGCTGG GTTTCATTTT	780
	AATACCTTGT TGATTTCACC AACTGTTGCT GGAAGATTCA AACTGGAAG CAAAACTTG	840
30	CTTGATTTTT TTTCTTGTT AACGTAATAA TAGAGACATT TTTAAAAGCA CACAGCTCAA	900
	AGTCAGCCAA TAAGTCTTTT CCTATTTGTG ACTTTTACTA ATAAAAATAA ATCTGCCTGT	960
35	AAATTATCTT GAAGTCCTTT ACCTGGAACA AGCACTCTCT TTTTCACCAC ATAGTTTAA	1020
	CTTGACTTTC AAGATAATTT TCAGGGTTTT TGTGTGTGTT GTTTTTGTGTT TGTGTGTTTT	1080
	GGTGGGAGAG GGGAGGGATG CCTGGGAAGT GGTAAACAAC TTTTTTCAAG TCACTTTACT	1140
40	AAACAAACTT TTGTAAATAG ACCTTACCTT CTATTTTCGA GTTTCATTTA TATTTGTCAG	1200
	TGTAGCCAGC CTCATCAAAG AGCTGACTTA CTCATTTGAC TTTTGCACTG ACTGTATTAT	1260
45	CTGGGTATCT GCTGTGTCTG CACTTCATGG TAAACGGGAT CTAAAATGCC TGGTGGCTTT	1320
	TCACAAAAAG CAGATTTTCT TCATGTACTG TGATGTCTGA TGCAATGCAT CCTAGAACAA	1380
	ACTGGCCATT TGCTAGTTTA CTCTAAAGAC TAAACATAGT CTTGGTGTGT GTGGTCTTAC	1440
50	TCATCTTCTA GTACCTTTAA GGACAAATCC TAAGGACTTG GACACTTGCA ATAAAGAAAT	1500
	TTTATTTTAA ACCCAAGCCT CCTGGATTG ATAATATATA CACATTTGTC AGCATTTCCG	1560
55	GTCGTGGTGA GAGGCAGCTG TTTGAGCTCC AATGTGTGCA GCTTTGAACT AGGGCTGGGG	1620
	TTGTGGGTGC CTCTCTGAA AGGTCTAACC ATTATTGGAT AACTGGCTTT TTTCTTCTC	1680
60	TTTGGAATGT AACAATAAAA ATAATTTTTG AAACATCAAA AAAAAAAAAA AAAA	1734

## (2) INFORMATION FOR SEQ ID NO: 109:

5

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 2003 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

10

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

	CGCAGGGGGC GCGCGGCCCG GGGACTCGCA TTCCCCGGTT CCCCCTCCAC CCCACGGGGC	60
15	CTGGACCATG GACGCCAGAT GGTGGGCAGT GGTGGTGCTG GCTGCGTTCC CCTCCCTAGG	120
	GGCAGGTGGG GAGACTCCCG AAGCCCCCTCC GGAGTCATGG ACCCAGCTAT GGTTCCTCCG	180
20	ATTTGTGGTG AATGCTGCTG GCTATGCCAG NITTTATGGTA CCTGGCTACC TCCTGGTGCA	240
	GTACTTCAGG CGGAAGAAGT ACCTGGAGAC CGGTAGGGGC CTCTGCTTTC CCCTGGTGAA	300
	AGCTTGTGTG TTTGGCAATG AGCCCAAGGC CTCTGATGAG GTTCCCCTGG CGCCCCGAAC	360
25	AGAGGCGGCA GAGACCACCC CGATGTGGCA GGCCCTGAAG CTGCTCTTCT GTGCCACAGG	420
	GCTCCAGGTG TCTTATCTGA CTTGGGGTGT GCTGCAGGAA AGAGTGATGA CCCGACGCTA	480
	TGGGGCCACA GCCACATCAC CGGGTGAGCG CTTTACGGAC TCGCAGTTCC TGGTGCTAAT	540
30	GAACCGAGTG CTGGCACTGA TTGTGGCTGG CCTCTCCTGT GTTCTCTGCA AGCAGCCCCG	600
	GCATGGGGCA CCCATGTACC GGTACTCCTT TGCCAGCCTG TCCAATGTGC TTAGCAGCTG	660
35	GTGCCAATAC GAAGCTCTTA AGTTCGTGAG CTTCCCCACC CAGGTGCTGG CCAAGGCCTC	720
	TAAGGTGATC CCTGTCATGC TGATGGGAAA GCTTGTGTCT CGGCGCANTA ACGAACACTG	780
	GGAGTACCTG ACAGCCACCC TCATCTCCAT TGGGGTCAGC ATGTTTCTGC TATCCAGCGG	840
40	ACCAGAGCCC CGCAGCTCCC CAGCCACCAC ACTCTCAGGC CTCATCTTAC TGGCAGGTTA	900
	TATTGCTTTT GACAGCTTCA CCTCAAAGTG GCAGGATGCC TGTTTGCCTA TAAGATGTCA	960
45	TCGGTGCAAG TGATGTTTGG GGTCAATTTC TTCTCCTGCC TCTTCACAGT GGGSTCACTG	1020
	CTAGNAACAG GGGGMCCTA CTGGAGGGAA CCCGCTTCAT GGGGCGACAC AGTGAGTTTG	1080
	CTGCCCATGC CCTGCTACTC TCCATCTGCT CCGCATGTGG CCAGCTCTTC ATCTTTTACA	1140
50	CCATGGGGCA GTTTGGGGCT GCCGTCTTCA CCATCATCAT GACCCTCCGC CAGGCCTTTG	1200
	CCATCCTTCT TTCCTGCCTT CTCTATGGCC AACTGTACAC TGTGGTGGGA GGGCTGGGGG	1260
55	TGGCTGTGGT CTTTGCTGCC CTCCTGCTCA GAGTCTACGC GCGGGGCCGT CTAAAGCAAC	1320
	GGGGAAAGAA GGCTGTGCCT GTTGAGTCTC CTGTGCAGAA GGTGTGAGGG TGGAAAGGGC	1380
60	CTGAGGGGTG AAGTGAAATA GGACCCTCCC ACCATCCCCT TCTGCTGTAA CCTCTGAGGG	1440

AGCTGGCTGA AAGGGCAAAA TGCAGGTGTT TTCTCAGTAT CACAGACCAG CTCTGCAGCA 1500  
 GGGGATTGGG GAGCCCAGGA GGCAGCCTTC CCTTTTGCCT TAAGTCACCC ATCTTCCAGT 1560  
 5 AAGCAGTTTA TTCTGAGCCC CGGGGGTAGA CAGTCCTCAG TGAGGGGTTT TGGGGAGTTT 1620  
 GGGGTCAAGA GAGCATAGGT AGGTTCACCA GTTACTCTTC CCACAAGTTC CCTTAAGTCT 1680  
 10 TGCCCTAGCT GTGCTCTGCC ACCTTCCAGA CTCACTCCCC TCTGCAAATA CCTGCATTTC 1740  
 TTACCCTGGT GAGAAAAGCA CAAGCGGTGT AGGCTCCAAT GCTGCTTTCC CAGGAGGGTG 1800  
 AAGATGGTGC TGTGCTGAGG AAAGGGGATG CAGAGCCCTG CCCAGCACCA CCACCTCCTA 1860  
 15 TGCTCCTGGA TCCCTAGGCT CTGTTCATG AGCCTGTTGC AGGTTTGGT ACTTTAGAAA 1920  
 TGTAACTTTT TGCTCTTATA ATTTTATTTT ATTAAATTAA ATTACTGCAA AAAAAAAAAA 1980  
 AAAAAAATCG GGGGGGGGCC CGN 2003  
 20

(2) INFORMATION FOR SEQ ID NO: 110:

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1320 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

30

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

GCTGAGCTGC CTTGAGGTGC AGTGTGGGG ATCCAGAGCC ATGTGGGACC TGCTACTACT 60  
 35 GGGCCTGATT GGGGGCCTGA CTCTCTTACT GCTGCTGACG CTGCTGGCCT TGCCCGGTA 120  
 CTCAGGGCTA CTGGCTGGGG TGGAAGTGAG TGCTGGGTCA CCCCCATCC GCAACGTCAC 180  
 40 TGTGGCCTAC AAGTTCCACA TGGGGCTCTA TGGTGAGACT GGGCGGCTTT TCACTGAGAG 240  
 CTGCAGCATC TCTCCAAGC TCCGCTCCAT CGCTGTCTAC TATGACAACC CCCACATGGT 300  
 GCCCCCTGAT AAGTGCCGAT GTGCCGTGGG CAGCATCCTG AGTGAAGGTG AGGAATCGCC 360  
 45 CTCCCCTGAG CTCATCGACC TCTACCAGAA ATTTGGCTTC AAGGTGTTCT CCTTCCCGGC 420  
 ACCCAGCCAT GTGGTGACAG CCACCTTCCC CTACACCACC ATTCTGTCCA TCTGGCTGGC 480  
 50 TACCCGCCGT GTCCATCCTG CCTTGACAC CTACATCAAG GAGCGGAAGC TGTGTGCCTA 540  
 TCCTCGGCTG GAGATCTACC AGGAAGACCA GATCCATTTC ATGTGCCCAC TGGCASGGCA 600  
 GGGAGACTTC TATGTGCCTG AGATGAAGGA GACAGAGTGG AAATGGCGGG GGCTTGTGGA 660  
 55 GGCCATTGAC ACCCAGGTGG ATGGCACAGG AGCTGACACA ATGAGTGACA CGAGTTCTGT 720  
 AAGCTTGAA GTGAGCCCTG GCAGCCGGGA GACTTCAGCT GCCACACTGT CACCTGGGGC 780  
 60 GAGCAGCCGT GGCTGGGATG ACGGTGACAC CCGCAGCGAG CACAGCTACA GCGAGTCAGG 840

5 TGCCAGCGGC TCCTCTTTTG AGGAGCTGGA YTTGGAGGGC GAGGGGCCCT TAGGGGAGTC 900  
 ACGGCTGGAC CCTGGGACTK AGCCCCTGGG GACTACCAAG TGGCTCTGGG AGCCCACTGC 960  
 CCCTGAGAAG GGCAAGGAGT AACCCATGGC CTGCACCCTC CCTGCAGTGC AGTTGCTGAG 1020  
 GAACTGAGCA GACTCTCCAG CAGACTCTCC AGCCCTCTTC CTCCTTCCTC TGGGGGAGGA 1080  
 10 GGGGTTCCTG AGGGACCTGA CTTCCCCTGC TCCAGGCCTC TTGCTAAGCC TTCTCCTCAC 1140  
 TGCCCTTTAG GCTCCCAGGG CCAGAGGAGC CAGGGACTAT TTCTTGCAAC CAGCCCCCAG 1200  
 GGCTGCCNCC CCTGTGTGT CTMTTMTTCA GACTCACAGT GGAGCTTCCA GGACCCAGAA 1260  
 15 TAAAGCCAAT GATTTACTTG TTTCAAAAAA AAAAWAAAAA AAAAAAAAAA AAAAAAAAAA 1320

20

(2) INFORMATION FOR SEQ ID NO: 111:

(i) SEQUENCE CHARACTERISTICS:

25

- (A) LENGTH: 1962 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

30

CGGACCCCTT CCTCCTCCTC NAAGCATGTC CCACCATGTG GGCAGGGGCT GGGGANACAG 60  
 TCACCTGATG CGGGGACCAC GGCCACTCCA CCTCGSTGGC GCTGTCTAGT GGCAGCACTG 120  
 35 GCTGGGCCTG CACTGAGGTC CCTGCTGGGG CAGTTCTTCC AGAATTATCT TCAGAGGGGG 180  
 CCTCCAGCTC CCTGGTACCC TCAGGGGCCC GTGTGGCTGG AAGCAGGGAA GGGGCACCCT 240  
 CGGAGCTTCC TGTCTCCTCG CTCTCTCCTC GAGGGACCCC AGATAGCTCA GGACCACCAG 300  
 40 TTGCCTCCCC CACCTCTCTT GCCTCAACCA GAGTGAAGG TGATGGGGAT GCTAGGTTCC 360  
 TCTCCCTGGG AGTGGGCAGA GTCTCAGTAG GTGGTCCATG GACCCTTGGA GGCTGGAAG 420  
 45 CTTCTGACTC TCCATCAGGA AGTGGTGATG CACCAGGCTG CAGGACTGCC CTTGCTGGCG 480  
 CCTGGGAGAG TGA CTCTCTCC TGGGCTGCTG GCTCAGTGGG GAGAGAGGCC TCAGGGCCCC 540  
 GGCTGCTGAG CTCGCTGGGC CATGCCACA GAGCCTCATC CTCACCTCC TCCTCTTCTT 600  
 50 CTTCTCTCTC TTTCTCTTCT TCATCTTCAT ATTTCTCTTC TTCTTCCAAT GCCTTACCTT 660  
 CCTCTTYTGR AAACCCCGTG GGCGGTACCA TGGATTGTGT TTCAAATTCT AGGACCTTCC 720  
 55 TAGGGGCCTC TGCTGGGTCT TCTGGAGTGG AGCTTCCACC TCCTTCTGTC TCCATGATGG 780  
 GGATGGAGTA RATGGCCCCA CGGGATTAC TCTCTGTGGC TTCCTGAGGC AGCTGCAGTT 840  
 60 CCTCCAGGGT CTCTGTCACT GTGACRATAG CCTCTAGTCC ATCAAAGCT GGGTTGGAGG 900

	CTGGGTGGA GGCCTCAGG ATGGCAGAAG GCTGGGCCGA GTCTCGGAAG CAGTARACGT	960
	TGAAGCGGCT GTGCTTATTG GGAAGCCAG TCTGGTTGGG GAAGANGAAG AGAGTCTTGA	1020
5	CACCAGGCAA GCGCCACCA CAGCGCTGGC TGGGTGTGAC GATGGGGTAG CGCACANTGC	1080
	CATCAGCTAG CCACCTGGGC TGCAGTGGTC CAGGCCACCA TCCCAGGCTG CATACAGTTG	1140
10	GCCCGTGGTG GCAATCTCTG CACCCCGCTC CTGGCAGTAC GCCCGTGCTT CCTCCAATGT	1200
	CAGCTTCTCT GGAGGGTCAC CCAGGAACAG TTCTCCATTT AGGTCTTCAG CATAACAGTA	1260
	CACATCATAG AGGTCATCCG GGTCCACCAC ACCATAGTTC CGGACCCCGG GGAAGCCATC	1320
15	CATGTCTCCG TAACAGGCCT CTCGTGGGGT CTGGATGGGA TACCTTTGAC CTTGAMCTCC	1380
	ACAGCGTCGC TGCTGTCTATC GATGCCGTGC TGGACCTCAC AGCGATAGAT ACCTGAGTCG	1440
20	TTGGGGCGCA GCTCGCTCAG CGCCAGGGGA GACGTCGGTG AGCGACGCTG GGTACGCAGG	1500
	CAGTGCCACG CGGAACCGGT AGGCCCTCGTT CACCTTGACG CGCACTCCCC GCGCCACCAG	1560
	CACYTCTGCC TCCCGGCCCC GGGACAGGAA AGTCCACTTG ACCCGCGGAG AGCCCAGCAC	1620
25	AGCCCGGCGG CTCGGCGGTG SCCGCAGGTA GTGGACGTGG CAAGGGATGK TGAGGGCSCC	1680
	GCCGAGCAAC GCCYTGCAGT GGCGCGTCGC CCGCGATGCG CACGCGAAAA GCGCGKTCCT	1740
30	CTGAGCTGTC TCCTTCCAGA ACATCTGCTA AAGCTGCAGG AGCCTGGGCC AGGACCAGGG	1800
	CTGCCAGCAG GGGCAGGAAC AGCTGGGCCA TGCTGCAGGC TACCCAGGGC TGGGGTTGGG	1860
	TCGCGGCACT GCGAAGTTTG TCGCCTCCTC CGGGGGTCTC CTCCGGGTTC ACGGCTCAGT	1920
35	NCCTGCAGCT GCAGCTGAGA CTGCGGCGGA GACTGCGCGA GC	1962

40 (2) INFORMATION FOR SEQ ID NO: 112:

(i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 1785 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

50	AAGTTTCAGC CAAACTTCGG GCGGCTGAGG CGGCGGCCGA GGAGCGGCGG ACTCSGGGCG	60
	CGGGGAGTCG AGGCATTTGC GCCTGGGCTT CGGAGCGTAC GCGAGGGCCT GAGCCTTTGA	120
55	AQCAGGAGGA GGGGAGGAGA GAGTGGGGCT CCTCTATCGG GACCCCTCC CCATGTGGAT	180
	CTGCCCAGGC GCGGCGGCG GCGGAGGAGG CGACCGAGAA GATRCCCGCC CTGCGCCCCG	240
	CTCTGCTGTG GCGGCTGCTG GCGCTCTGGC TGTGCTGCGC GACCCCGCGC ATGCATTGCA	300

	GTGTCGAGAT GGCTATGAAC CCTGTGTAAA TGAAGGAATG TGTGTTACCT ACCACAATGG	360
	CACAGGATAC TGCAAATGTC CAGAAGGCTT CTTGGGGGAA TATTGTCAAC ATCGAGACCC	420
5	CTGTGAGAAG AACCGCTGCC AGAATGGTGG GACTTGTGTG GCCCAGGCCA TGCTGGGGAA	480
	AGCCACGTGC CGATGTGCCT CAGGGTTTAC AGGAGAGGAC TGCCAGTACT CGACATCTCA	540
10	TCCATGCTTT GTGTCTCGAC CTTGCCTGAA TGGCGGCACA TGCCATATGC TCAGCCGGGA	600
	TACCTATGAG TGCACCTGTC AAGTCGGGTT TACAGGTAAG GAGTGCCAAT GGACCGATGC	660
	CTGCCTGTCT CATCCCTGTG CAAATGGAAG TACCTGTACC ACTGTGGCCA ACCAGTTCTC	720
15	CTGCAAATGC CTCACAGGCT TCACAGGGCA GAAGTGTGAG ACTGATGTCA ATGAGTGTGA	780
	CATTCCAGGA CACTGCCAGC ATGGTGGCAC CTGCCTCAAC CTGCCTGGTT CCTACCAGTG	840
20	CCAGTGCCTT CAGGGCTTCA CAGGCCAGTA CTGTGACAGC CTGTATGTGC CCTGTGCACC	900
	CTCGCCTTGT GTCAATGGAG GCANCTGTG GCAGACTGGT GACTTCACIT TTGAGTGCAA	960
	CTGCCTTCCA GAAACAGTGA GAAGAGGAAC AGAGCTCTGG GAAAGAGACA GGAAGTCTG	1020
25	GAATGGAAAA GAACACGATG AGAATTAGAC ACTGGAAAAT ATGTATGTGT GGTTAATAAA	1080
	GTGCTTTAAA CTGAATTGAC ATTAACAGTR GGTGATCAAC TTMTCTATGT GCTTGTGCTT	1140
30	TTGCTTTTGA TGGAGTAATT CATTGTTTTC TTATCCACCT AAATGCACCC AGCTGCCCTT	1200
	GATTTTCTCT GGGCTACTGG CCTTCACAAC CCTCTCCCAT GTACCCTCTC TGACTTTGGG	1260
	GTAACCTCC CCTAACTTAA AGCTAGAGAA TTCTGAACT GAGGAGGGGA TCCTCTGTTA	1320
35	ATCAGTGAGC ACTTTTGTAT GAGCTGATAG ATGATATATG AGAGACTATG CGTGGCACAA	1380
	TACTTTGTTA CACTCTTCAC TGATACAAGT GTTCTAGAGT GYACACACAA CCCAAAGATA	1440
40	GAAATAAAAA GAGGAGCAGT GTCGGGGAGC TTGGGGCCTG GTGTTCCATG GAGAGGGAGA	1500
	AAGGAACAAG CTTGRCCAAT TCATTCAACT CTTATAAAA ATGATGAGGA GGCTGAAAAC	1560
	CAAGAATTTT GATTGGGAAC AGAATACAAG CAGCTGAAKC AGATGAWTTA CTAAGCAACA	1620
45	AAGATCCTGT TTTTATACAA ATATCCTTAG TACAAAAACA AAARAAGGAA AACTGTAGGG	1680
	GGGAGTAATG TGCTAAGTAA GCAGAATGTC CTCCAAAAGA AGTGTGTTCT AGTTACTCTT	1740
50	TTCCGGGTNG GGATCTTTAG NTTCCGTAT TGTGGGTATG GTTCC	1785

## (2) INFORMATION FOR SEQ ID NO: 113:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1842 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

5	GGAGCCTCTC TTGCAACTTC TGCCACCGCG GGCCACCGCG GCCGCCTGAT CCCGCAGAGG	60
	AAGTCGCGGC CGTGGAGCGA TGACCCGCGG CGGTCCGGGC GGGCGCCCGG GGCTGCCACA	120
	GCCGCGCCCG CTTCCTGCTGC TGCTGCTGCT GCMGCTGTTG TTAGTCACCG CGGAGCCGCC	180
10	GAAACCTGCA GGAGTCTACT ATGCAACTGC ATACTGGATG CCTGCTGAAA AGACAGTACA	240
	AGTCAAAAAT GTAATGGACA AGAATGGGGA CGCCTATGGC TTTTACAATA ACTCTGTGAA	300
15	AACCACAGGC TGGGGCATCC TGGAGATCAG AGCTGGCTAT GGCTCTCAAA CCCTGAGCAA	360
	TGAGATCATC ATGTTTGTGG CTGGCTTTT TGGAGGGTTAC CTCACTGCCC CACACATGAA	420
	TGACCACTAC ACAAACCTCT ACCCACAGCT GATCACGAAA CCTTCCATCA TGGATAAAGT	480
20	GCAGGATTTT ATGGAGAAGC AAGATAAGTG GACCCGGAAA AATATCAAAG AATACAAGAC	540
	TGATTCATTT TGGAGACATA CAGGCTATGT GATGGCACAA ATAGATGGCC TCTATGTAGG	600
25	AGCAAAGAAG AGGGCTATAT TAGAAGGGAC AAAGCCAATG ACCCTGTTCC AGATTCAAGT	660
	CCTGAATAGT GTTGGAGATC TATTGGATCT GATTCCCTCA CTCTCTCCCA CAAAAACGG	720
	CAGCCTAAAG GTTTTTAAGA GATGGGACAT GGGACATTGC TCCGCTCTTA TCAAGGTTCT	780
30	TCCTGGATTT GAGAACATCC TTTTGTCTCA CTCAAGCTGG TACACGTATG CAGCCATGCT	840
	CAGGATATAT AAACACTGGG ACTTCAACRT CATAGATAAA GATACCAGCA GTAGTCGCCT	900
35	CTCTTTCAGC AGTTACCCAG GGTTTTGTGA GTCTCTGGAT GATTTTACCA TTCTTAGCAG	960
	TGGATTGATA TTGCTGCAGA CCACAAACAG TGTGTTTAAT AAAACCCTGC TAAAGCAGTA	1020
	ATACCCGAGA CTCTCCTGTC CTGGCAAAGA GTCCGTGTGG CCAATATGAT GGCAGATAGT	1080
40	GGCAAGAGGT GGGCAGACAT CTTTTCAAAA TACAACTCTG GCACCTATAA CAATCAATAC	1140
	ATGGTCTCTG ACCTGAAGAA AGTAAAGCTG AACCACAGTC TTGACAAAGG CACTCTGTAC	1200
45	ATTGTGGAGC AAATTCCTAC ATATGTAGAA TATTCTGAAC AAAGTATGT TCTACGGA	1260
	GGATATTGGC CCTCCTACAA TGTTCCTTTC CATGAAAAAA TCTACAAC TGAGTGGCTAT	1320
	CCACTGTTAG TTCAGAAGCT GGGCTTGGAC TACTCTTATG ATTTAGCTCC ACGAGCCAAA	1380
50	ATTTTCCGGC GTGACCAAGG GAAAGTGA CTGATACGGCAT CCATGAAATA TATCATGCGA	1440
	TACAACAATT ATAAGAAGGA TCCTTACAGT AGAGGTGACC CCTGTAATAC CATCTGCTGC	1500
55	CGTGAGGACC TGAACCTACC TAACCCAAAGT CCTGGAGGTT GTTATGACAC AAAGGTGGCA	1560
	GATATCTACC TAGCATCTCA GTACACATCC TATGCCATAA GTGGTCCAC AGTACAAGGT	1620
	GGCCTCCCTG TTTTTCGCTG GGACCGTTTC AACAAAAC TCATATCAGG CATGSCAGAG	1680
60	GTCTACAAC TTTGATTTTAT TACCATGAAA CCAATTTTGA AACTTGATAT AAAATGAAGG	1740



5 AGGGAGATGA CGACTAGAA GACTGTAAAT AAGATACCAA AGGCACTATT TTAGCTATGT 1800  
 TTTTCCCATC AGAATTATGC AATAAAATAT ATTAATTTGT CA 1842

10 (2) INFORMATION FOR SEQ ID NO: 114:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1960 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

20 GAATTCGGCA CGAGCTTCTC CGCGCCCCAG CCGCCGGCTG CCAGCTTTTC GGGGCCCCGA 60  
 GTCGCACCCA GCGAAGAGAG CCGGCCCCGG ACAAGCTCGA ACTCCGGCCG CCTCGCCCTT 120  
 CCCC GGCTCC GCTCCCTCTG CCCCCTCGGG GTCGCGCGCC CACGATGCTG CAGGGCCCTG 180  
 25 GCTCGTGCT GCTGCTCTTC CTCGCCTCGC ACTGCTGCCT GGGCTCGGCG CGCGGGCTCT 240  
 TCCTCTTTGG CCAGCCCGAC TTCTCCTACA AGCGCAGMAA TTGCAAGCCC ATCCCGGTCA 300  
 ACCTGCAGCT GTGCCACGGC ATCGAATACC AGAACATGCG GCTGCCCAAC CTGCTGGGCC 360  
 30 ACGAGACCAT GAAGGAGGTG CTGGAGCAGG CCGGCGCTTG GATCCCGCTG GTCATGAAGC 420  
 AGTGCCACCC GGACACCAAG AAGTTCCTGT GTCGCTCTT CGCCCCGTC TGCTTCGATG 480  
 35 ACCTAGACGA GACCATCCAG CCATGCCACT CGCTCTGCGT GCAGGTGAAG GACCGCTGCG 540  
 CCCC GGTCAT GTCCGCCTTC GGNITCCCCCT GGCCCCACAT GCTTGAGTGC GACCGTTTCC 600  
 CCCAGGACAA CGACCTTTGC ATCCCCCTCG CTAGCAGCGA CCACCTCCTG CCAGCCACCG 660  
 40 AGGAAGCTCC AAAGGTATGT GAAGCCTGCA AAAATAAAAA TGATGATGAC AACGACATAA 720  
 TGGAAACGCT TTGTAAAAAT GATTTTGCAC TGAAAATAAA AGTGAAGGAG ATAACCTACA 780  
 45 TCAACCGAGA TACCAAAATC ATCCTGGAGA CCAAGAGCAA GACCATTTAC AAGCTGAACG 840  
 GTGTGTCCGA AAGGGACCTG AAGAAATCGG TGCTGTGGCT CAAAGACAGC TTGCAGTGCA 900  
 CCTGTGAGGA GATGAACGAC ATCAACGCGC CCTATCTGGT CATGGGACAG AAACAGGGTG 960  
 50 GGGAGCTGGT GATCACCTCG GTGAAGCGGT GGCAGAAGGG GCAGAGAGAG TTCAAGCGCA 1020  
 TCTCCCGCAG CATCCGCAAG CTGCAGTGCT AGTCCCGGCA TCCTGATGGC TCCGACAGGC 1080  
 55 CTGCTCCAGA GCACGGCTGA CCATTTCTGC TCCGGGATCT CAGCTCCCGT TCCCCAAGCA 1140  
 CACTCCTAGC TGCTCCAGTC TCAGCCTGGG CAGCTTCCCC CTGCCTTTTG CACGTTTGCA 1200  
 60 TCCCCAGCAT TTCCTGAGTT ATAAGGCCAC AGGAGTGGAT AGCTGTTTTC ACCTAAAGGA 1260

AAAGCCCACC CGAATCTTGT AGAAATATTC AAATAATAA AATCATGAAT ATTTTATGA 1320  
 AGTTTAAAAA TAGCTCACTT TAAAGCTAGT TTTGAATAGG TGCAACTGTG ACTTGGGTCT 1380  
 5 GGTGTTTGT TGTGTTGT TTTGAGTCAG CTGATTTTCA CTTCCCACTG AGGTTGTCAT 1440  
 AACATGCAAA TTGCTTCAAT TTTCTCTGTG GCCCAAACCTT GTGGGTCACA AACCCGTGTG 1500  
 10 AGATAAAGCT GGTGTTATC TCAACATCTT CATCAGCTCC AGACTGAGAC TCAGTGTCTA 1560  
 AGTCTTACAA CAATTCATCA TTTTATACCT TCAATGGGAA CTTAACTGT TACATGTATC 1620  
 ACATTCCAGC TACAATACTT CCATTTATTA GAAGCACATT AACCATTCT ATAGCATGAT 1680  
 15 TTCTCAAGT AAAAGGCAAA AGATATAAAT TTTATAATTG ACTTGAGTAC TTTAAGCCTT 1740  
 GTTTAAACA TTTCTTACTT AACTTTTGCA AATTAAACCC ATTGTAGCTT ACCTGTAATA 1800  
 TACATAGTAG TTTACCTTTA AAAGTTGTAA AAATATTGCT TTAACCAACA CTGTAAATAT 1860  
 20 TTCAGATAAA CATTATATTC TTGTATATAA ACTTTACATC CTGTTTACC TAAAAAATAA 1920  
 AAAAAAATAA AAAAAACTCG AGGGGGGCCC GGTACCCAAT 1960

25

## (2) INFORMATION FOR SEQ ID NO: 115:

30

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 536 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

35

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

GTGCTCAGCC CCCGGGCAC AGYAGGACGT TTGGGGGCCT TCTTTCAGCA GGGGACAGCC 60  
 40 CGATTGGGGA CAATGGCGTC TCTTGCCAC ATCTTGGTTT TCTGTGTGGG TCTCCTCACC 120  
 ATGGCCAAGG CAGAAAGTCC AAAGGAACAC GACCCGTTCA CTTACGACTA CCAGTCCCTG 180  
 45 CAGATCGGAG GCCTCGTCAT CGCCGGGATC CTCTTCATCC TGGGCATCCT CATCGTGCTG 240  
 AGCAGAAGAT GCCGGTGCAA GTTCAACCAG CAGCAGAGGA CTGGGGAACC CGATGAAGAG 300  
 GAGGGAACTT TCCGCAGCTC CATCCGCCGT CTGTCCAMCC GCANGCGGTA GAAACACCTG 360  
 50 GAGCGATGGA ATCCGGCCAG GACTCCCTG GCACCTGACA TCTCCACGC TCCACCTGCG 420  
 CGCCACCGC CCCCTCGCC GCCCTTCCC CAGCCCTGCC CCCGCAGACT CCCCTGCGC 480  
 55 CCAAGACTTC CAATAAAACG TCGTTCTCTC TCGAMAAAAA AAAAAATAAA AAAACT 536

## (2) INFORMATION FOR SEQ ID NO: 116:

60

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 790 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

5

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

10 GTGGGGAGGG GCGGAGCAA AGCCGCGCCT CTGGGTGGGC GGGTCGGGCC GTCCAGGTCC 60  
 CTGACTTGAA CTTTCCCGGT CCCAGCCCT CAACAGGAGG CGCAGAAAAT CTTCAAAGCC 120  
 AACCACCCCA TGGACGCAGA AGTTACTAAG GCCAAGCTTC TGGGGTTTGG CTCTGCTCTC 180  
 15 CTGGACAATG TGGACCCCAA CCCTGAGAAC TTCGTGGGGG CGGGGATCAT CCAGACTAAA 240  
 GCCCTGCAGG TGGGCTGTCT GCTTCGGCTG GAGCCCAATG CCCAGGCCCA GATGTACCGG 300  
 CTGACCCTGC GCACCAGCAA GGAGCCCGTC TCCCGTCACC TGTGTGAGCT GCTGGCACAN 360  
 20 AGTTCTGAGC CTTGGACTCT GCCCCGGGGG ATGTGGCCCG CACTGGGCAG CCCCTTGGAC 420  
 TGAGGCAGTT TTGTGGATG GGGGACCTCC ACTGGTGACA GAGAAGACAC CAGGGTTTGG 480  
 25 GGGATGCCTG GGACTTTCCT CCGGCCTTTT GTATTTTAT TTTTGTTCAT CTGCTGCTGT 540  
 TTACATTCTG GGGGTTAGG GGGAGTCCCC CTCCCTCCCT TCCCCCACA AGCACAGAGG 600  
 GGAGAGGGGC CAGGGAAGTG GATGTCTCCT CCCCTCCAC CCCACCCTGT TGTAGCCCT 660  
 30 CCTACCCCT CCCCATCCAG GGGCTGTGTA TTATGTGAG CGAATAAACA GAGAGACGTT 720  
 AACAGCCCCA TGTCTGTGTC CATCACCCAN TGNTAGGTAG TCAAAGAAGT GGGGTGAGGG 780  
 35 CATGCAGAGT 790

## 40 (2) INFORMATION FOR SEQ ID NO: 117:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 776 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

45

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

50 CAGCGCTGGA AGCAGCTGAG CCTGTGAGGG GTGGGGAGGG GCGGAGCAA AGCCGCGCCT 60  
 CTGGGTGGGC GGGTCGGGCC GTCCAGGTCC CTGACTTGAA CTTTCCCGGT CCCAGCCCT 120  
 CAACAGGAGG CGCAGAAAAT CTTCAAAGCC AACCACCCCA TGGACGCAGA AGTTACTAAG 180  
 55 GCCAAGCTTC TGGGGTTTGG CTCTGCTCTC CTGGACAATG TGGACCCCAA CCCTGAGAAC 240  
 TTCGTGGGG CGGGGATCAT CCAGACTAAA GCCCTGCAGG TGGGCTGTCT GCTTCGGCTG 300  
 60 GAGCCCAATG CCCAGGCCCA GATGTACCGG CTGACCCTGC GCACCAGCAA GGAGCCCGTC 360

1 TCCCCTCACC TGTGTGAGCT GCTGGCACAG AGTTCTGAGC CCTGGACTCT GCCCGGGGG 420  
5 ATGTGGCCGG CACTGGGCAG CCCCTTGGAC TGAGGCAGTT TTGGTGGATG GGGGACCTCC 480  
ACTGGTGACA GAGAAGACAC CAGGGTTTGG GGGATGCCTG GGACTTTCCT CCGGCCTTTT 540  
GTATTTTAT TTTTGTTCAT CTGCTGCTGT TTACATTCTG GGGGGTTAGG GGGAGTCCCC 600  
10 CTCCCTCCCT TTCCCCCCA AGCACAGAGG GGAGAGGGGC CAGGGAAGTG GATGTCTCCT 660  
CCCCTCCAC CCCACCCTGT TGTAGCCCCT CCTACCCCCT CCCCATCCAG GGGCTGTGTA 720  
15 TTATTGTGAG CGAATAAACA GAGAGACCN TAAAAAATA AAAAAAAT TGAGGG 776

20 (2) INFORMATION FOR SEQ ID NO: 118:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 453 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
25 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

30 GGTTCGACA CCAGATGTTT TCTGCTCCTG GTTAATGTCA GTGAGGGCTG GAAGTTGAAT 60  
AAATGAGAAC AGGAGTGGTC TGGGCCCATG TAAATGATCC TCCCTTGAAA GGAGGAACAG 120  
CTTTCATCAT TTGTTCCAGC TAAGCCTTGC ATGCATTATA GATCTGGTGC TAAGCAGTGG 180  
35 GAAAGATCTC ATAAGTAATG TTTTATGTTT TTTCKGTCTC TCYTCTTCKG TTGTTCTTGG 240  
CTTGTGGGTT GTGTTTGKGG TTGTTAACTG GAAATTTGCT ATAAGCCAGT TGTCTYCKAAK 300  
TTTWAAAAAC GAATTAGAAA AACCATAAAA TCYTCTGGCC YATGCACATK GTCCCYGTTT 360  
40 TGTGAAACA TTAAAGGTA AATAAAAAGG AAGGAGAACA GTCAATAATG TGCATCAAAT 420  
ATATTCTGAG TTCTAGAGAA ATTAATGACC AAG 453

45

(2) INFORMATION FOR SEQ ID NO: 119:

50 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2016 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
55 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

AGGCTGTTCA CAGGCACCCC GAGACAGCGT CCCCCCTCTG GCGCACTGG ATTTGACGTT 60  
60 GCAGGACGCG CGGCTGGAAC CCCAGGCC CGCTGCTCAC AGACCGGGAC TCCGCTCCG 120

	GTTCCCGAGG GCGTGGCGAG GCGCTGCGGG ANCCCAACAG GATGCCTTCC GTGCCTTCCA	180
5	TCAAGATCTC AATTTTGTGC GCAATTCTTA CAGCCCCTGT TGATTGGAGA GCTGGCTCCG	240
	GAAGAACCCA GCCAKGATGG ACCCCTGAAT GCGCATGGTC GAGGACTTCC GAGCCCCTGCA	300
	CCAGGCAGCC GAGGACATGA AGCTGTTTGA TGCCAGTCCC ACCTTCTTTG CTTTCTACT	360
10	GGGCCACATC CTGGCCATGG AGGTGCTGGC CTGGCTCCTT ATCTACCTCC TGGGTCTGG	420
	CTGGGTGCCC AGTGCCCTGG NCCGCTTCA TCCTGGCCAT CTCTCAGGCT CAGTCCTGGT	480
15	GTCTGCAGCA TGACCTGGGC CATGCTCCAT CTTCAAGAAG TCCTGGTGGA ACCACGTGGC	540
	CCAGAAGTTC GTGATGGGGC AGCTAAAGGG CTTCTCCGCC CACTGGTGGA ACTTCCGCCA	600
	CTTCCAGCAC CACGCCAAGC CCAACATCTT CCACAAAGAC CCAGACGTGA CGGTGGCGCC	660
20	CGTYTTCCTC CTGGGGGAGT CATCCGTCGA GTATGNNCAA GAAGAAACGC AGATACCTAC	720
	CCTACAACCA GCAGCACCTG TACTTCTTCC TGATCGGCCC GCCGCTGCTC ACCCTGGTGA	780
25	ACTTTGAAGT GGAAAATCTG GCGTACATGC TGGTGTGCAT GCAGTGGGCG GATTTGCTCT	840
	GGGCCGCCAG CTTCTATGCC CGCTTCTTCT TATCCTACCT CCCCTTCTAC GGCGTCCCTG	900
	GGGTGCTGCT CTTCTTTGTT GCTGTGAGGT ATGGCAGGGA GTGGCGAGGT CACACACAGG	960
30	CGACAGGTGA CCCCCACTGC AGCCCCCAC CAGAGCTTCC CTTTTCCCGT CTGCAGAATG	1020
	GGGCCAGTGG TACTGCCTCC CTGGCTTGCT GGTGGAATCA CATAAACACA AGYTTCAAGG	1080
35	GCCCAGGGTC GGTGGGTTTA GGGAGCGTGG CCTGGCTTGT AAGTGGCCCG GTGGGTGTCG	1140
	GAGCTGCTCT GGA CTGAGCC TCACAGTGGA CACTGCTCCA TTCAGATTCT TTAAACACTG	1200
	GCAAGGGGGC GATGGCCACA ATCCTATTGT ACAGATAAGG AAGTCAAGGC CAYTTGGGGA	1260
40	CAGYTGCTCT TCCAGCCTCC ACTCAGGGTG CCTTAAGTGG TGAGCTGGAC CTAGGGCAGT	1320
	GCCGAGCTC CACACAGGGT CCTGGAAGC CACTGGTTTC TGTGGATCAC ACAGATGAAC	1380
45	CACATCCCCA AGGAGATCGG CCACGAGAAG CACCGGACT GGGTCAGCTC TCAGCTGGCA	1440
	GCCACCTGCA ACGTGGAGCC CTCACTTTTC ACCAACTGGT TCAGCGGGCA CCTCAACTTC	1500
	CAGATCGAGC ACCACCTCTT CCCCAGGATG CCGAGACACA ACTACAGCCG GGTGGCCCCG	1560
50	CTGGTCAAGT CGCTGTGTGC CAAGCACGGC CTCAGCTACG AATGAAGCCC TCCTCACCG	1620
	CGCTGGTGGA CATCGTCAGG TCCCTGAAGA AGTCTGGTGA CATCTGGCTG GACGCCTACC	1680
55	TCCATCAGTG AAGGCAACAC CCAGGCGGGC AGAGAAGGGC TCAGGGCACC AGCAACCAAG	1740
	CCAGCCCCCG GCGGGATCGA TACCCCCAMC CCTCCACTGG CCAGCCTGGG GGTGCCCTGC	1800
	CTGCCCTCCT GGTACTGTTG TCTTCCCTC GGGCCCTCA CATGTGTATT CAGCAGCCCT	1860
60	ATGGCCTTGG CTCTGGGCCT GATGGGACAG GGGTAGAGGG AAGGTGAGCA TAGCACATTT	1920

5 TCCTAGAGCG AGAATTGGGG GAAAGCTGTT ATTTTATAT TAAAATACAT TCAGATGTAA 1980  
 AAAAAAAAAA AAAAAAANCT CGAGGGGGG CCCC GG 2016

10 (2) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 2136 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

20 GGGGACGGAG CCGCTGTCAA CTCTCCTCACT CAGCTCAGCT GATCGGTTGC CGCCGCCGCC 60  
 GCCGCCAGAT TCTGGAGGCG AAGAACGCAA AGCTGAGAAC ATGGACGTTA ATATCGCCCC 120  
 ACTCCGCGCC TGGGACGATT TCTTCCCGGG TTCCGATCGC TTGCCCCGGC CGGACTTCAG 180  
 25 GGACATTTC AAATGGAACA ACCGCGTAGT GAGCAACCTG CTCTATTACC AGACCAACTA 240  
 CCTGGTGGTG GCTGCCATGA TGATTTCAT TGTGGGGTTT CTGAGTCCCT TCAACATGAT 300  
 CCTGGGAGGA ATCGTGGTGG TGCTGGTGT CACAGGGTTT GTGTGGGCAG CCCACAATAA 360  
 30 AGACGTCCTT CGCCGGATGA AGAAGCGCTA CCCCACGACG TTCGTTATGG TGGTCATGTT 420  
 GCGGAGCTAT TTCCTTATCT CCATGTTTGG AGGAGTCATG GTCCTTGTGT TTGGCATTAC 480  
 35 TTTTCCTTTG CTGTTGATGT TTATCCATGC ATCGTTGAGA CTTCGGAACC TCAAGAACAA 540  
 ACTGGAGAAT AAAATGGAAG GAATAGGTTT GAAGAGGACA CCGATGGGCA TTGTCTTGGA 600  
 TGCCCTAGAA CAGCAGGAAG AAGGCATCAA CAGACTCACT GACTATATCA GCAAAGTGAA 660  
 40 GGAATAAACA TAACTTACCT GAGCTAGGGT TGCAGCAGAA ATTGAGTTGC AGCTTGCCCT 720  
 TGTCCAGACC TATKTTCTGC TTGCGTTTGT GAAACAGGAG GTGCACGTAC CACCCAATTA 780  
 45 TCTATGGCAG CATGCATGTA TAGGCCGAAC TATTATCAGC TCTGATGTTT CAGAGAGAAG 840  
 ACCTCAGAAA CCGAAAGAAA ACCACCACC TCCTATTGTG TCTGAAGTTT CACGTGTGTT 900  
 TATGAAATCT AATGGGAAAT GGATCACACG ATTTCTTTAA GGAATTAAA AAAAAATAAA 960  
 50 GAATTACGGC TTTTACAGCA ACAATACGAT TATCTTATAG GAAAAAAAAA ATCATGTGTA 1020  
 ACTATCAAGA CAATACGAGT AAATGAAAAG GCTGTTAAAG TAGATGACAT CATGTGTTAG 1080  
 55 CCTGTTCTTA ATCCCCTAGA ATTGTAACT GTGGGATATA AATTAGTTTT TATTATCTC 1140  
 TTAAAAATCA AAGATGATCT CTATCACTTT GCCACCTGTT TGATGTGCAG TGGAACTGG 1200  
 60 TTAAGCCAGT TGTTCACT TCSTTTACAA ATATAAGAT AGCTGTTTAG GATATTTTGT 1260

265

TACATTTTGTG TAAATTTTGTG AAATGCTAGT AATGTGTTTT CACCAGCAAG TATTTGTTGC 1320  
 AAACCTTAATG TCATTTTCCT TAAGATGGTT ACAGCTATGT AACCTGTATT ATTCTGGACG 1380  
 5 GACTTATTAA AATACAAACA GACAAAAAAT AAAACAAAAC TTGAGTTCTA TTTACCTTGC 1440  
 ACATTTTGTG TTGTTACAGT GAAAAAATG GTCCAAGAAA ATGTTTGCCA TTTTTCATT 1500  
 GTTTCGTTTT TAACTGGAAC ATTTAGAAAG AAGGAAATGA ATGTGCATTT TATTAATTCC 1560  
 10 TTAGGGGCAC AAGGAGGACA ATAATAGCTG ATCTTTTGAA ATTTGAAAAA CGTCTTTAGA 1620  
 TGACCAAGCA AAAAGACTTT AAAAAATGGT AATGAAAATG GAATGCAGCT ACTGCAGCTA 1680  
 15 ATAAAAAATT TTAGATAGCA ATTGTTACAA CCATATGCCT TTATAGCTAG ACATTAGAAT 1740  
 TATGATAGCA TGAGTTTATA CATTCTATTA TTTTCTCTCC CTTTCTCATG TTTTATAAA 1800  
 TAGGTAATAA AAAATGTTTT GCCTGCCAAT TGAATGATTT CGTAGCTGAA GTAGAAACAT 1860  
 20 TTAGGTTTCT GTAGCATTAA ATTGTGAAGA CAACTGGAGT GGTACTTACT GAAGAAACTC 1920  
 TCTGTATGTC CTAGAATAAG AAGCAATGAT GTGCTGCTTC TGATTTTCT TGCATTTTAA 1980  
 25 ATTCTCAGCC AACCTACAGC CATGATCTTT AGCACAGTGA TATCACCATG ACTTCACAGA 2040  
 CATGGTCTAG AATCTGTACC CTTACCCACA TATGAAGAAT AAAATTGATT AAAGGTTAA 2100  
 AAAAAAWAA AAAAMWAGG GGGGCCCGGT WCCAG 2136  
 30

(2) INFORMATION FOR SEQ ID NO: 121:

35

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 219 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

GCCCTAGTAT CTGGGCAGCT GTGCATGGAG ATAGCCAGAG GAAACATTTT TTTTCTTAAT 60  
 45 GRATGTGTA CCACATTTTG TTGTTCTTGC CTCCTATTAT CCGTGCSCA TTTGCATSCT 120  
 GGTTCCTTCT ACAGTAGTTT ATGTAAATGT TGTTTGTCC TTGTCGTTCT CAGTAGAATT 180  
 50 GGTTCGTGTA ACGAAACCTG GTCCTGTAAT TTCAGTATA 219

55

(2) INFORMATION FOR SEQ ID NO: 122:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1686 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double

60

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

5	GCTGGAGATT CACATTTTAC CTGATTGCCT TCATTGCCCG CATGGCCGTC ATTGTGGATA	60
	AACCCCTGGTT CTATGACATG AAGAAAGTTT GGGAGGGATA TCCCATACAG AGCACTATCC	120
	CTTCCCAGTA TTGGTACTAC ATGATTGAAC TTTCCTTCTA CTGGTCCCTG CTCCTTCAGCA	180
10	TTGCCCTCTGA TGTCAAGCGA AAGGATTTC AAGAACAGAT CATCCACCAT GTGRCCACCA	240
	TCATTCTCAT CAGCTTTTCC TGGTTTGCCA ATTACATCCG AGCTGGGACT CTAATCATGG	300
15	CTCTGCATGA CTCTTCOGAT TACCTGCTGG AGTCAGCCAA GATGTTTAAC TACGCGGGAT	360
	GGAAGAACAC CTGCAACAAC ATCTTCATCG TCTTCGCCAT TGTTTTATC ATCACCCGAC	420
	TGGTCATCCT GCCCTTCTGG ATCCTGCATT GCACCCCTGGT GTACCCACTG GAGCTCTATC	480
20	CTGCCCTTCTT TGGSTATTAC TTCTTCAATT CCATGATGGG AGTTCTACAG CTGCTGCATA	540
	TCTTCTGGGC CTACCTCATT TTGCGCATGG CCCACAAGTT CATAACTGGG AAAGCTGGTA	600
25	GAAGATGAAC GCAWGCRCGG GNAAGAAACA GAGAGCTCAG AGGGGGAGGA GGCTGCAGCT	660
	GGGGGAGGAG CAAAGAGCCG GCCCCTAGCC AATGGCCACC CCATCCTCAA TAACAACCAT	720
	CGTAAGAATG ACTGAACCAT TATTCCAGCT GCCTCCCAGA TTAATGCATA AAGCCAAGGA	780
30	ACTACCCYGC TCCCTGCGCT ATAGGGTCAC TTTAAGCTCT GGGGAAAAG GAGAAAGTGA	840
	GAGGAGAGTT CTCTGCATCC TCCCTCCTTG CTTGTACACC AGTTGCCTTT AAACCAAATT	900
35	CTAACCAGCC TATCCCAGG TAGGGGGACG TTGGTTATAT TCTGTTAGAG GGGGACGGTC	960
	GTATTTTCTT CCCTACCCGC CAAGTCATCC TTTCTACTGC TTTTGAGGCC CTCCCTCAGC	1020
	TCTCTGTGGG TAGGGGTTAC AATTCACATT CCTTATTCTG AGAATTGGC CCCAGCTGTT	1080
40	TGCCCTTGAC TCCCTGACCT CCAGAGCCAG GGTGTGCCT TATTGTCCCA TCTGTGGGCC	1140
	TCATTCTGCC AAAGCTGGAC CAAGGCTAAC CTTTCTAAGC TCCCTAACTT GGGCCAGAAA	1200
45	CCAAAGCTGA GCTTTTAACT TTCTCCCTCT ATGACACAAA TGAATTGAGG GTAGGAGGAG	1260
	GGTGCACATA ACCCTTACCC TACCTCTGCC AAAAAGTGGG GGCTGTACTG GGGACTGCTC	1320
	GGATGATCTT TCTTAGTGCT ACTTCTTTCA GCTGTCCCTG TAGCGACAGG TCTAAGATCT	1380
50	GACTGCCTCC TCCTTCTCTT GGCCTCTTCC CCCTTCCCTC TTCTCTTCAG CTAGGCTAGC	1440
	TGTTTGGAG TAGAATGGCA ACTAATTCTA ATTTTATTTT ATTAAATATT TGGGGTTTGG	1500
55	GTTTAAAGC CAGAATTACG CCTAGCACCT AGCATTTTCAG CAGAGGGACC ATTTTAGACC	1560
	AAAATGTACT GTTAATGGGT TTTTPTTAA AATTAAAGA TTAAATAAAA AATATTAAAT	1620
60	AAAACATGGC AATAAGTGTC AGACTATTAG GAATTGAGAA GGGGGATCAA CTAAATAAAC	1680



GAAGAG

1686

5

(2) INFORMATION FOR SEQ ID NO: 123:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 1211 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

15

CAGCCTGTGC CAGACGAGGA GGTGATTGAG CTGTATGGGG GTACCCAGCA CATCCCACTA 60

TACCAGATGA GTGGCTTCTA TGGCAAGGGT CCCTCCATTA AGCAGTTCAT GGACATCTTC 120

20

TCGCTACCGG AGATGGCTCT GCTGTCCTGT GTGGTGGACT ACTTCTGGG CCACAGCCTG 180

GAGTTTGACC AAACATCTCT ACAAGGACGT GACGGACGCC ATCCGAGACG TGCATGTGAA 240

GGGCCTCATG TACCAGTGGG TCGAGCAGGA CATGGAGAAG TACATCCTGA GAGGGGATGA 300

25

GACGTTTGCT GTCTGAGCC GCCTGGTGGC CCATGGGAAA CAGCTGTTC TCATCACCAA 360

CAGTCTTTC AGCTTCGTAG ACAAGGGGAT GCGGCACATG GTGGGTCCCG ATTGGCGCCA 420

30

CTCTTCGATG TGGTCATTGT CCAGGCAGAC AAGCCCAGCT TCTTCACTGA CCGGCGCAAC 480

TTTCAGAAAA CTCGATGAGA AGGGCTCACT TCAGTGGGAC CGGATCACCC GCTTGGAAAA 540

GGGCAAGATC TATCGGCAGG GAAACCTGTT TGACTTCTTA CGCTTGACGG AATGGCCTGG 600

35

CCCCCGCTG CTCTACTTCG GGGACCACCT CTATAGTGAT CTGGCGGATC TCATGCTGCG 660

GCACGGCTGG CGCACAGGCG CCATCATCCC CGAGCTGGAG CGTGAGATCC GCATCATCAA 720

40

CACGGAGCAG TACATGCACT CGCTGACGTG GCAGCAGGCG CTCACGGGCG TGCTGGAGCG 780

CATGCAGACC TATCAGGACG CGGAGTCGAG GCAGGTGCTG GCTGCCTGGA TGAAAGAGCG 840

GCAGGAGCTG AGGTGCATCA CCAAGGCCCT GTTCAATGCG CAGTTCGGCA GCATCTTCCG 900

45

CACCTTCCAC AACCCACCT ACTTCTCAAG GCGCCTCGTG CGCTTCTCTG ACCTCTACAT 960

GGCCTCCCTC AGCTGCCTGC TCAACTACCG CGTGGACTTC ACCTTCTACC CAGCCCGTAC 1020

50

GCCGCTGCAG CACGAGGCAC CCCTCTGGAT GGACCAGCTT CTGCACCGGC TGCATGAAGA 1080

CCCCCTTCCT TGGTGACATG GCCACATCC GCTGAGGGCA CCTTTATTGT CTGGGACAGG 1140

CCCTCAGCCC CTCCTGCCCC ATCCACCCAG ACAAGCAATA AAAGTGGTCT CCTCCCTGAA 1200

55

AAAAAAAAA A 1211

60

## (2) INFORMATION FOR SEQ ID NO: 124:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1804 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

10	CGCACCTATG GGCTCGCTAC CAGGACATGC GGAGACTGGT GCACGACCTC CTGCCCCCGG	60
	AGGTCTGCAG TCTCCTGAAC CCAGCAGCCA TCTACGCCAA CAACGAGATC AGCCTGCGTG	120
15	ACGTTGAGGT CTACGGCTTT GACTACGACT ACACCCTGGC CCAGTATGCA GACGCACTGC	180
	ACCCCCGAGAT CTTCACTACC GCCCGTGACA TCCTGATCGA GCACTACAAG TACCCAGAAG	240
20	GGATTCGGAA GTATGACTAC AACCCCAGCT TTGCCATCCG TGGCCTCCAC TATGACATTC	300
	AGAAGAGCCT TCTGATGAAG ATTGACGCCT TCCACTACGT GCAGCTGGGG ACAGCCTACA	360
	GGGGCCTCCA GCCTGTGCCA GACGAGGAGG TGATTGAGCT GTATGGGGT ACCCAGCACA	420
25	TCCCACTATA CCAGATGAGT GGCTTCTATG GCAAGGGTCC CTCCATTAAG CAGTTCATGG	480
	ACATCTTCTC GCTACCGGAG ATGGCTCTGC TGTCTGTGT GGTGGACTAC TTTCTGGGCC	540
	ACAGCCTGGN AGTTTGACCA AGCACATCTC TACAAGGACG TGACGGACGC CATCCGAGAC	600
30	GTGCATGTGA AGGGCCTCAT GTACCAGTGG ATCGAGCAGG ACATGGAGAA GTACATCCTG	660
	AGAGGGGATG AGACGTTTGC TGTCTGAGC CGCCTGGTGG CCCATGGGAA ACAGCTGTTC	720
35	CTCATCACCA ACAGTCCTTT CAGCTTCGTA GACAAGGGGA TCGGCACAT GGTGGGTCCC	780
	GATTGGCGCC ACTCTTCGAT GTGGTCATTG TCCAGGCAGA CAAGCCCAGC TTCTTCACTG	840
40	ACCGGCGCAA GCTTTTCAGA AAACCTCGATG AGAAGGGCTC ACTTCAGTGG GACCGGATCA	900
	CCCGCTTGGA AAAGGGCAAG ATCTATCGGC AGGGAAACCT GTTTGACTTC TTACGCTTGA	960
	CGGAATGGCG TGGCCCCCGC GTGCTCTACT TCGGGGACCA CCTCTATAGT GATCTGGCGG	1020
45	ATCTCATGCT GCGGCACGGC TGGCGCACAG GCGCCATCAT CCCCAGCTG GAGCGTGAGA	1080
	TCCGCATCAT CAACACGGAG CAGTACATGC ACTCGCTGAC GTGGCAGCAG GCGCTCACGG	1140
50	GGCTGCTGGA GCGCATGCAG ACCTATCAGG ACGCGGAGTC GAGGCAGGTG CTGGCTGCCT	1200
	GGATGAAAGA GCGGCAGGAG CTGAGGTGCA TCACCAAGGC CCTGTTC AAT GCGCAGTTG	1260
	GCAGCATCTT CCGCACCTTC CACAACCCCA CCTACTTCTC AAAGGCGCCT CGTGCGCTTC	1320
55	TCTGACCTCT ACATGGCCTC CCTCAGCTGC CTGCTCAACT ACCGCGTGA CTTCACCTTC	1380
	TACCCACGCC GTACGCCGCT GCAGCACGAG GCACCCCTCT GGATGGACCA GCTCTGCACC	1440
60	GGCTGCATGA AGACCCCTT CCTTGGTGAC ATGGCCACA TCCGCTGAGG GCACCTTTAT	1500

TGTCTGGGAC AGGCCCTCAG CCCCTCCTGC CCCATCCACC CAGACAAGCA ATAAAAGTGG 1560  
 TCTCCTCCCT GTGCATGCTT CTGCTTTCAG CCCCAGCCTC GTCACCTGAC TGTGAGGATC 1620  
 5 CTCTGGGTGT CAGGGAAGTC CTCCTCCAGC AGTGAGTCAT CGAAGGGTTC ACAAAGGTG 1680  
 TCGCTGCCAA AGACAGGGTT GGGGACAGAG ACCAGGGTGG GGTGGTCCC TTCTTGCCAC 1740  
 10 GGTGAGAAGT CGTCGTCAGC CGGACGCGTG GGTGACCCG GGAATTCCGG ACCGGTACCT 1800  
 GCAG 1804

15

(2) INFORMATION FOR SEQ ID NO: 125:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1282 base pairs  
 20 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

CCGCAGGNCA GCGACGCGAC TCTGGTGCGG GCCGTCTTCT TCCCCCGAG CTGGGCGTGC 60  
 GCGGCCGCAA TGAAGTGGGA GCTGCTGCTG TGGCTGCTGG TGCTGTGCGC GCTGCTCCTG 120  
 30 CTCTTGGTGC AGCTGTGCG CTCTCTGAGG GCTGACGGCG ACCTGACGCT ACTATGGGCC 180  
 GAGTGGCAGG GACGACGCC AGAATGGGAG CTGACTGATA TGGTGGTGTG GGTGACTGGA 240  
 35 GCCTCGAGTG GAATTGGTGA GGAGCTGGCT TACCAGTTGT CTAAACTAGG AGTTTCTCTT 300  
 GTGCTGTCAG CCAGAAGAGT GCATGAGCTG GAAAGGGTGA AAAGAAGATG CCTAGAGAAT 360  
 GGCAATTTAA AAGAAAAAGA TATACTTGT TGGCCCTTG ACCTGACCGA CACTGGTTCC 420  
 40 CATGAAGCGG CTACCAAGC TGTCTCCAG GAGTTTGGTA GAATCGACAT TCTGGTCAAC 480  
 AATGGTGGAA TGTCCCAGCG TTCTCTGTGC ATGGATACCA GCTTGGATGT CTACAGAAAG 540  
 CTAATAGAGC TTAAGTACTT AGGGACGGTG TCCTTGACAA AATGTGTTCT GCCTCACATG 600  
 45 ATCGAGAGGA AGCAAGGAAA GATTGTTACT GTGAATAGCA TCCTGGGTAT CATATCTGTA 660  
 CCTCTTTCCA TTGGATACTG TGCTAGCAAG CATGCTCTCC GGGGTTTTTT TAATGGCCTT 720  
 50 CGAACAGAAC TTGCCACATA CCCAGGTATA ATAGTTTCTA ACATTTGCCC AGGACCTGTG 780  
 CAATCAAATA TTGTGGAGAA TTCCCTAGCT GGAGAAGTCA CAAAGACTAT AGGCAATAAT 840  
 GGAGACCACT CCCACAAGAT GACAACCAGT CGTTGTGTGC GGCTGATGTT AATCAGCAIG 900  
 55 GCCAATGATT TGAAAGAAGT TTGGATCTCA GAACACCTT TCTTGTAGT AACATATTTG 960  
 TGGCAATACA TGCCAACCTG GGCCTGGTGG ATAACCAACA AGATGGGGAA GAAAAGGATT 1020  
 60 GAGAACTTTA AGAGTGGTGT GGATGCAGAC TCTCTTATT TTAAATCTT TAAGACAAA 1080

CATGACTGAA AAGAGCAYCT GTACTTTTCA AGCCACTGGA GGGARAAATG GAAAACATGA 1140  
 AAACAGCAAT CTTCTTATGC TTCTGAATAA TCAAAGACTA ATTTGTGRTT TTACTTTTTA 1200  
 ATAGATATGA CTTTGCTTCC AACATGGAAT GAAATAAAAA ATAAATAATA AAAGATTGCC 1260  
 ATGGAAAAAA AAAAGNNGGG AN 1282

10

## (2) INFORMATION FOR SEQ ID NO: 126:

15

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1296 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

20

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

GGCAGAGCTT AGAGTGTGGA AAAGGCAACC AGGTGGCCG TAAGTGCCTG CTGGAATGCG 60  
 TGTGCCTCCA CASGGRTCTG GGCATCCGGA CTGATAACCA GCCGGCCAGA CTGAGGGATG 120  
 GAAGGCACTG AGATGGGGGC CCGTCCAGGC GGACACCCGC AGAAATGGAG CTTTCTGTGG 180  
 TCTCTTGAC TCTGGCTGCC TCTGGCCCTC TCTGTGTCTC TCTTTCTTGG TCTCTCCCTC 240  
 TCTCCTCCTC AGCCTGGTCT TTCTCTTTGG TGCACACTTA GTTATTGTTG TGAGCAATGG 300  
 AAGTTCAAAG GAACTCCCTC TCCAGCTCTT CTGAATCTTG GGACACAGCC TAAAAGGAC 360  
 AAAAAGTTAG AAGACAGCAT AGCAACTCAG CTCAGGGRGC TACCAGAGAA AAATAGCAAC 420  
 TGATGTGGGT GCTTTTTTTT TTTTCTTAAT TTGAATAAAA AGAATTAGAA GTGATGTCCT 480  
 TTTATAAAAT GCCTTCTCCC CCTTCCCGCC TACAGTCTCT TCCTCTCCCC TTAGAGGGGG 540  
 GAAAGTGTAT AAACCTACAG GGTGTGAGT CTGAAAAGAG GATCCCCCTC ACCCCCACCC 600  
 TGGCAGAGC AGTGGGGGTT GGGGGGTGGG AGAGGGGGAC ACAGATCCTG GCACACTGTG 660  
 GATATTTCTT GCAGATTGCA GTCTCTTGTG GCCCAAACAG GTTAGGTAGA CTATCGCCTC 720  
 TGGCAGGTGC CACCTTTTGG TACCAACATG TTCTGAGGTG TTAGGATTG GGTGGGTTT 780  
 TTTTGTGTTG TTTTTTTTTT CCMTTGGTC TTTTTTTTTT TCYCCTTKTA AAGAAAAGCT 840  
 AAAGGCCGCT GTGAGTCCTG GTGCAGGCT CTCCATGGAT GTAGCATATC GAAGATAATT 900  
 TTTATACTGC ATTTTATGAG ATTATTTTGT AATGTGTGAT TCCGTCTGCT GAGGAGGTGG 960  
 GAGGGGCTCC AGGGAAAGCC ACCCACCTTC AGTGAGGTG CTCCCGAGCT GAGCGCACCG 1020  
 GGCATGGGAT GTGGAGGCTG GCGACACACC CTGTGCCTCT CCAAGGCTGG GCGCGTGGGG 1080  
 CGTCCAGAGT CTCTCTGGGT CTCAGATGTC CATCTGCCAC CTCTTGTTAA GGCTCTAGCC 1140

60

271

AGAAGGGAGG GTGAGGGTAG AAGAAAGTTA TTCCCGAAGA AAAAAAGAAT GAAAAGTCAT 1200  
 TGTACTGAAC TGTTTTTATA TTTTAAAAAG TTACTATTTA AAGCGGACGT CGTGGGTCGA 1260  
 5 CCCGGGAATT CCCGGACCGG TACTGTCAGG TCTAAC 1296

10 (2) INFORMATION FOR SEQ ID NO: 127:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 737 base pairs  
 (B) TYPE: nucleic acid  
 15 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

20 GGCANAGTGG AGGCAATGCC AGCTCCAGGA CAGAGGCTCA GGTGCCCAAC GGGCAAGGCA 60  
 GCCCAGGGGG CTGTGTCTGT TCAAGTCAGG CTTCCCGGC CCYTCGCGCA NCAGCGCTTC 120  
 CACGGGCAGC CCGGGGCCCC ACCCCACGCA CTGAAGAGGC CGCCTGGGCT GCCATGGCCC 180  
 25 TGACCTTCCT GCTGGTGCTG CTCACCTGG CCACGCTCTG CACACGGCTG CACAGAACT 240  
 TCCGACGCGG GGAGAGCATC TACTGGGGGC CCACAGCGGA CAGCCAGGAC ACAGTGGCTG 300  
 30 CTGTGCTGAA GCGGAGGCTG CTGCAGCCCT CGCGCCGGT CAAGCGCTCG CGCCGGAGAC 360  
 CCYTCYTCCC GCCCAGCCG GACAGCGGCC CGGAAGGCGA GAGCTCGGAG TGACGGCCTG 420  
 GGACCTGCCA CTGTGGCGTG CGGTCTCCCC GCGCCGCGAG GCCGCGAMCT NTGCCACGTG 480  
 35 GACCGCGCGC NGGCGCTMC CCTGTGGCG ATGGCGCGC ACTGGCGAGC ACTGCGKGGG 540  
 CTTTCCTCCT TGTGTGTTGC TGAGTGGGCG GCCAAGGGGA GAAAAGGAGC CGCTTYTGCC 600  
 40 TCCCTTGCCA AAACTCGTT TCTAATTAA TTTTTTTAG TAGAAAAAA AAAAAAAA 660  
 AAAAAAAA AAAAAAAA AAAAAAAC TCGAGGGGG GCCCGGTACC CAATTNGCCA 720  
 AATAGCGATC GTATNAA 737  
 45

50 (2) INFORMATION FOR SEQ ID NO: 128:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1925 base pairs  
 (B) TYPE: nucleic acid  
 55 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

60 CCCCGCCTCC AAAGCTAACC CTCGGGCTTG AGGGGAAGAR GCTGACTGTA CGTTCCTTCT 60

	ACTCTGGCAC CACTCTCCAG GCTGCCATGG GGCCAGCAC CCCTCTCCTC ATCTTGTTCC	120
	TTTTGTTCATG GTCGGGACCC CTCCAAGGAC AGCAGCACCA CCTTGTTGGAG TACATGGAAC	180
5	GCCGACTAGC TGCTTTAGAG GAACGGCTGG CCCAGTGCCA GGACCAGAGT AGTCGGCATG	240
	CTGCTGAGCT GCGGGACTTC AAGAACAAGA TGCTGCCACT GCTGGAGGTG GCAGAGAAGG	300
10	AGCGGGAGGC ACTCAGAACT GAGGCCGACA CCATCTCCGG GAGAGTGGAT CGTCTGGAGC	360
	GGGAGGTAGA CTATCTGGAG ACCCAGAACC CAGCTCTGCC CTGTGTAGAG TTTGATGAGA	420
	AGGTGACTGG AGGCCCTGGG ACCAAAGGCA AGGGAAGAAG GAATGAGAAG TACGATATGG	480
15	TGACAGACTG TGGCTACACA ATCTCTCAAG TGAGATCAAT GAAGATTCTG AAGCGATTTG	540
	GTGGCCGAGC TGGTCTATGG ACCAAGGATC CACTGGGGCA AACAGAGAAG ATCTACGTGT	600
20	TAGATGGGAC ACAGAATGAC ACAGCCTTTG TCTTCCCAAG GCTGCGTGAC TTCACCCTTG	660
	CCATGGCTGC CCGGAAAGCT TCCCGAGTCC GGGTGCCCTT CCCCTGGGTA GGCACAGGC	720
	AGCTGGTATA TGGTGGCTTT CTTTATTTTG CTCGGAGGCC TCCTGGAAGA CCTGGTGGAG	780
25	GTGGTGAGAT GGAGAACACT TTGCAGCTAA TCAAATTCCA CCTGGCAAAC CGAACAGTGG	840
	TGGACAGCTC AGTATTCCA GCAGAGGGGC TGATCCCCC CTACGGCTTG ACAGCAGACA	900
30	CCTACATCGA CCTGGCAGCT GATGAGGAAG GTCTTTGGGC TGTCTATGCC ACCCGGAGG	960
	ATGACAGGCA CTTGTGTCTG GCCAAGTTAG ATCCACAGAC ACTGGACACA GAGCAGCAGT	1020
	GGGACACACC ATGTCCCAGA GAGAATGCTG AGGCTGCCTT TKTCACTCTGT GGGACCCTCT	1080
35	ATGTCGTCTA TAACACCCGT CCTGCCAGTC GGGCCCGCAT CCAGTGCTCC TTTGATGCCA	1140
	GCGGACCCTG ACCCCTGAAC GGGCAGCACT CCCTTATTTT CCCCGCAGAT ATGGTGCCCA	1200
40	TGCCAGCTC CGCTATAACC CCCGAGAAG CCAGCTCTAT GCCTGGGATG ATGGCTACCA	1260
	GATTGTCTAT AAGCTGGAGA TGAGGAAGAA AGAGGAGGAG GTTTGAGGAG CTAGCCTTGT	1320
	TTTTTGATC TTTCTCACTC CCATACATTT ATATTATATC CCCACTAAAT TTCTTGTTCC	1380
45	TCATTCTTCA AATGTGGGCC AGTTGTGGCT CAAATCCTCT ATATTTTTAG CCAATGGCAA	1440
	TCAAATCTTT TCAGCTCCTT TGTTCATAC GGAAGTCCAG ATCCTGAGTA ATCCTTTTAG	1500
50	AGCCCGAAGA GTCAAAACCC TCAATGTTCC CTCCTGCTCT CCTGCCCCAT GTCAACAAAT	1560
	TTGAGGCTAA GGATGCCCCA GACCCAGGGC TCTAACCTTG TATGCGGGCA GGCCAGGGA	1620
	GCAGGCAGCA GTGTCTTCC CTTAGAGTG ACTTGGGAG GGAGAAATAG GAGGAGACGT	1680
55	CCAGCTCTGT CCTCTCTTCC TCACTCCTCC CTTCAAGTGC CTGAGGAAQA GGACTTTCTC	1740
	CACATTGTTT TGTATTGCAA CATTTTGCAT TAAAGGAAA ATCCAMAAAA AAAAAAAAAA	1800
60	AAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA	1860

ACTGCGGCCG CTGTCCCTTC TGTCGTCTTC TCGCAGCCGT ACCCTTCTGT CGTCTTCTCG 1920  
CAGCC 1925

5

(2) INFORMATION FOR SEQ ID NO: 129:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2713 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

TCCTACCTTC CCAACCCTCT GGCATCCCCA GCACTGATGG TCCTGGCATC CACGGCTGAG 60  
GCCAGCCGTG ACTGCTTCCA TCCCTTGTC A GAGCCACGA CCCTTTGGTG TACCTGTGTC 120  
AGTTGACAAG GACGTGCATA TTCCTTTCAC CAACGGTTCC TATACCTTTG CCTCTATGTA 180  
CCATCGGCAA GGTGGGGTGC CAGGCACTTT TGCCAATCGT GATTTCCCCC CTTCTCTACT 240  
ACACCTCCAC CCTCAATTG CTCCCCAAA TCTAGATTGC ACCCCAATCA GTATGCTGAA 300  
TCATAAGTGG TGTGGGGGT TCCGGCCTTT GSCTCCACCC GRGGACCGGG RGAGYTATCA 360  
GTCAGCTTTA CGCCGGCCAA GCGACTTAAG AACTGCCATG ACACAGAGTC TCCCCACTTG 420  
CGCNTCTCAG ATGCAGATGG GAANGAATAT GACTTTGGGA CACAGCTGCM ATCTAGCTCC 480  
CCCGGTTTAC TAAAGGTTGA TGACACTGGG AAGAAGATTT TTGCTGTCTC TGGCCTCATT 540  
TCTGATCGGG AAGCCTCATC TAGCCAGAG GNTCGNAAT GACAGATGTA AGAAGAAAGC 600  
AGCGGCATTG TTCGACAGCC AGGCCCAAT TTGCCCCATC TGCCAGGTCC TGCTGAGGCC 660  
CAGTGAGCTG CAGGAGCATA TGGAGCAGGA ACTGGAGCAG CTAGCCCAAC TGCCCTCGAG 720  
CAAGAATTCC CTTCTGAAGG ATGCCATGGC TCCAGGCACC CCAAAGTCCC TCCTGTTGTC 780  
TGCTTCCATC AAGAGGGAAG GAGAGTCTCC AACGGCATCA CCCCACTCAT CTGCCACCGA 840  
TGACCTCCAC CATTCAGACA GATACCAGAC CTTTCTGCGA GTACGAGCCA ACCGGCAGAC 900  
CCGAYTGAAT GYTGGGATTG GGAAAATGAA ACGGAGGAAG CAAGATGAAG GGCAGGTATG 960  
TCCCCTGTGC AACCGCCCCC TGGCAGGATC GGAGCAGGAG ATGAGTAGGC ATGTGGAGCA 1020  
TTGCCTTTCT AAGAGGGAAG GCTCCTGCAT GGCTGAGGAT GATGCTGTGG ACATCGAGCA 1080  
TGAGAACAAC AACCGCTTTG AGGAGTATGA GTGGTGTGGA CAGAAGCGGA TACGGGCCAC 1140  
CACTCTCCTG GAAGGTGGCT TCCGAGGCTC TGGCTTCATC ATGTGCAGCG GAAAGAGAA 1200  
CCCGGACAGT GATGCTGACT TGGATGTGGA TGGGGATGAC ACTCTGGAGT ATGGGAAGCC 1260  
ACAATACACA GAGGCTGATG TCATCCCCTG CACAGGCGAG GAGCCTGGTG AAGCCAAGGA 1320

	GAGAGAGGCA	CTTCGGGGCG	CAGTCCTAAA	TGGCGGCCCT	CCCAGCACGC	GCATCACACC	1380
5	TGAGTTCTCT	AAATGGGCCA	GTGATGAGAT	GCCATCCACC	AGCAATGGTG	AAAGCAGCAA	1440
	GCAGGAGGCC	ATGCAGAAGA	CCTGCAAGAA	CAGCGACATC	GAGAAAATCA	CCGAAGATTC	1500
	AGCTGTGACC	ACGTTTGAGG	CTCTGAAGGC	TCGGGTGAGA	GAACCTGAAC	GGCAGCTATC	1560
10	TCGTGGGGAC	CGTTACAAAT	GCCTCATCTG	CATGGACTCG	TACTCGATGC	CCCTAACGTC	1620
	CATCCAGTGT	TGGCACGTGC	ACTGCGAGGA	GTGCTGGCTG	CGGACCCTGG	GTGCCAAGAA	1680
15	GCTCTGCCCT	CAGTGCAACA	CGATCACAGC	GCCCGGAGAC	CTGCGGAGGA	TCTACTGTG	1740
	AGCTATCTGC	CCCAGGCAGG	CCTCGCCTCC	AGCAGCCCCA	CCTGCCCCCA	GCCTCTGTGA	1800
	CAGTGACCGT	YTCCCTTTGT	ACATACTTGC	ACACAGGTTT	CCCATGTACA	TACATGCACA	1860
20	TACTCAAACA	TGCGTACACA	CACACACATT	TACACACGCA	GGACTCTGGA	GCCAGAGTAG	1920
	AGGCTGTGGC	CCAGGCACTA	CCTGCTGGCT	CCCACCTATG	GTTTGGGGGC	CATACCTGTT	1980
25	CCAGCTCTGT	TCCCAGGGTG	GGGCAGGGAG	GTGGGGGTTG	GGGGAGTAGT	GGGGCACGGC	2040
	TCCTAAGATC	CAGCCCCCAT	ACTGACAGAC	GGACAGACAG	ACATGCAAAC	ACCAGACTGA	2100
	AGCACATGTA	ATATAGACCG	TGTATGTTTA	CAATGTTGTG	TATAAATGGG	ACAACTCCTC	2160
30	GCCCTCTACC	TGTCCCTTCC	CCCTTTGGTT	GTATGATTTT	CTTCTTTTTT	AAGAACCCCT	2220
	GGAAGCAGCG	CCTCCTTCAG	GGTGGCTGG	GAGCTCGGCC	CATCCACCTC	TGGGGGTAYC	2280
35	TGCCTCTCTC	TCTCCTGTGG	TGTCCCTTCC	CTCTCCCATG	TGCTCGGTGT	TCAGTGGTGT	2340
	ATATTTCTTC	TCCCAGACAT	GGGGCACACG	CCCCAAGGGA	CATGATCCTC	TCCTTAGTCT	2400
	TAGCTCATGG	GGCTCTTTAT	AAGGAGTTGG	GGGGTAGAGG	CAGGAAATGG	GAACCGAGCT	2460
40	GAAGCAGAGG	CTGAGTTAGG	GGGCTAGAGG	ACAGTGCTCC	TGGCCACCCA	GCCTCTGCTG	2520
	AGAACCATTG	CTGGGATTAG	AGCTGCCTTT	CCCAGGGAAG	AAGTGTGCTC	TCCCCGACCC	2580
45	TCCCGTGGGC	CCTGTGGTGT	GATGCTGTGT	CTGTATATTC	TATACAAAGG	TACTTGTCTT	2640
	TTCCCTTTGT	AAACTACATT	TGACATGGAT	TAAACCAGTA	TAAACAGTTA	AAAAAAAAAA	2700
	AAAAAAAACT	CGA					2713
50							

(2) INFORMATION FOR SEQ ID NO: 130:

- 55 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1011 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: linear
- 60



## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

	AGAGGACGGT GTGACCCGGG AGGAAGTAGA GCCTGAGGAG GCTGAAGAAG GCATCTCTGA	60
5	GCAACCCTGC CCAGCTGACA CAGAGGTGGT GGAAGACTCC TTGAGGCAGC GTAAAAGTCA	120
	GCATGCTGAC AAGGGACTGT AGATTTAATG ATGCGTTTTC AAGAATACAC ACCAAAACAA	180
10	TATGTCAGCT TCCCTTGGC CTGCAGTTTG TACCAAATCC TTAATTTTTY YTGAATGAGC	240
	AAGCTTCTCT TAAAAGATGC TCTCTAGTCA TTTGGTCTCA TGGCAGTAAG CCTCATGTAT	300
	ACTAAGGAGA GTCTTCCAGG TGTGACAATC AGGATATAGA AAAACAAACG TAGTGTNTGG	360
15	GATCTGTTTG GAGACTGGGA TGGGAACAAG TTCATTTACT TAGGGGTCAG AGAGTCTCCA	420
	CCAGAGGAGG CCATTCCCAG TCCTAATCAG CACCTTCCAG AGACAAGGCT GCAGGCCCTG	480
	TGAAATGAAA GCCAAGCAGG AGCCTTGGCT CTGAGNCATC CCCAAAGTGT AACGTAGAAG	540
20	CCTTGCATCC TTTTCTGTG TAAAGTATTT ATTTTGTGCA AATTGCAGGA AACATCAGGC	600
	ACCACAGTGC ATGAAAATC TTTCACAGCT AGAAATTGAA AGGGCCTTGG GTATAGAGAG	660
25	CAGCTCAGAA GTCATCCCAG CCCTCTGAAT CTCCTGTGCT ATGTTTTATT TCTTACCTTT	720
	AATTTTCCA GCATTTCAC CATGGGCATT CAGGCTCTCC ACACTCTTCA CTATTATCTC	780
	TTGGTCAGAG GACTCCAATA ACAGCCAGGT TTACATGAAC TGTGTTTGT CATCTGACC	840
30	TAAGGGGTTT AGATAATCAG TAACCATAAC CCCTGAAGCT GTGACTGCCA AACATCTCAA	900
	ATGAAATGTT GTRGCCATCA GAGACTCAA AGGAAGTAAG GATTTTACAA GACAGATTAA	960
35	AAAAAATTG TTTTGTCCAA AAAANAAAAA AAAAAACTC GAAGGGGGG C	1011

## 40 (2) INFORMATION FOR SEQ ID NO: 131:

## (i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 2278 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

50	GTAATTCGGC ACGAGGCGCC CAACATGGCG GGTGGGCGCT GCGGCCCGCA SCTAACGGCG	60
	CTCCTGGCCG CTTGGATCGC GGCTGTGGCG GCGACGGCAG GCCCCGAGGA GGCCCGCTG	120
	CCGCCGGAGC AGAGCCGGGT CCAGCCCATG ACCGCCTCCA ACTGGACGCT GGTGATGGAG	180
55	GGCGAGTGA TGCTGAAATT TTACGCCCA TGGTGTCCAT CCGCCAGCA GACTGATTCA	240
	GAATGGGAGG CTTTTCGAAA GAATGGTGAA ATACTTCAGA TCAGTGTGGG GAAGGTAGAT	300
60	GTCATTCAAG AACCAGGTTT GAGTGGCCGC TTCTTTGTCA CCACTCTCCC AGCATTTTTT	360

	CATGCAAAGG ATGGGATATT CCGCCGTTAT CGTGGCCCAG GAATCTTCGA AGACCTGCAG	420
5	AATTATATCT TAGAGAAGAA ATGGCAATCA GTCGAGCCTC TGA CTGGCTG GAAATCCCCG	480
	GCTTCTCTAA CGATGTCTGG AATGGCTGGT CTTTTTAGCA TCTCTGGCAA GATATGGCAT	540
	CTTCACA ACT ATTTCACAGT GACTCTTGGA ATTCTCTGCTT GGTGTTCTTA TGTCTTTTTTC	600
10	GTCATAGCCA CCTTGGTTTT TGGCCTTTTT ATGGGTCTGG TCTTGGTGGT AATATCAGAA	660
	TGTTTCTATG TGCCACTTCC AAGGCATTTA TCTGAGCGTT CTGAGCAGAA TCGGAGATCA	720
15	GAGGAGGCTC ATAGAGCTGA ACAGTTGCAG GATGCGGAGG AGGAAAAAGA TGATTCAAAT	780
	GAAGAAGAAA ACAAGACAG CCTTGTAGAT GATGAAGAAG AGAAAGAAGA TCTTGGCGAT	840
	GAGGATGAAG CAGAGGAAGA AGAGGAGGAG GACAACTTGG CTGCTGGTGT GGATGAGGAG	900
20	AGAAGTGAGG CCAATGATCA GGGGCCCCCA GGAGAGGACG GTGTGACCCG GGAGGNAAGT	960
	AGAGCCTGAG GAGGCTGAAG AAGGCATCTC TGAGCAACCC TGCCAGCTG ACACAGAGGT	1020
25	GGTGGAAGAC TCCTTGAGGC AGCGTAAAAG TCAGCATGCT GNCAAGGGAC TGTAGATTTA	1080
	ATGATGCGTT TTCAAGAATA CACACCAAAA CAATATGTCA GCTTCCCTTT GGCCTGCAGT	1140
	TTGTACCAAA TCCTTAATTT TTCCTGAATG AGCAAGCTTC TCTTAAAAGA TGCTCTCTAG	1200
30	TCATTTGGTC TCATGGCAGT AAGCCTCATG TATACTAAGG AGAGTCTTCC AGGTGTGACA	1260
	ATCAGGATAT AGAAAAACAA ACGTAGTGTN TGGGATCTGT TTGGAGACTG GGATGGGAAC	1320
35	AAGTTCATTT ACTTAGGGGT CAGAGAGTCT CGACCAGAGG AGGCCATTC CAGTCCTAAT	1380
	CAGCACCTTC CAGAGACAAG GCTGCAGGCC TGTGAAATGA AAGCCAAGCA GGAGCCTTGG	1440
	CTCTGAGGCA TCCCAAAGT GTAACGTAGA AGCCTTGCAT CCTTTTCTTG TGTAAAGTAT	1500
40	TTATTTTTGT CAAATTGCAG GAAACATCAG GCACCACAGT GCATGAAAAA TCTTTTCACAG	1560
	CTAGAAATTG AAAGGGCCTT GGGTATAGAG AGCAGCTCAG AAGTCATCCC AGCCCTCTGA	1620
45	ATCTCTGTG CTATGTTTTA TTTCTTACCT TTAATTTTTT CAGCATTTCC ACCATGGGCA	1680
	TTCAGGCTCT CCACACTCTT CACTATTATC TCTTGGTCAG AGGACTCCAA TAACAGCCAG	1740
	GTTTACATGA ACTGTGTTTG TTCATTCTGA CCTAAGGGGT TTAGATAATC AGTAACCATA	1800
50	ACCCCTGAAG CTGTGACTGC CAAACATCTC AAATGAAATG TTGTRGCCAT CAGAGACTCA	1860
	AAAGGAAGTA AGGATTTTAC AAGACAGATT AAAAAAAT TGTTTTGTCC NAAAATATAG	1920
55	TTGTGTGTA TTTTTTTTTA AGTTTTCTAA GCAATATTTT TCAAGCCAGA ATCTCTCTAA	1980
	GTCTTGCCAG TALAAGGTAG TCTTGTGAAG AAAAGTTGAA TACTGTTTTG TTTTCATCTC	2040
	AAGGGGTTC CTGGGTCTTG AACTACTTTA ATAATACTA AAAAACCCT TCTGATTTTC	2100
60	CTTCAGTGAT GTGCTTTTGG TGAAAGAATT AATGAACTCC AGTACCTGAA AGTGAAAGAT	2160

TTGATTTTGT TTCCATCTTC TGTAATCTTC CAAAGAATTA TATCTTTGTA AATCTCTCAA 2220  
 TACTCAATCT ACTGTAAGTA CCCAGGGRGG STAATTTCTT TAAAAA AAAA 2278  
 5

10 (2) INFORMATION FOR SEQ ID NO: 132:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1088 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

20 GGCAGGGGCG GCGTGAACCC GTCGGGCACT GTGTCCCTGA CAATGGGAAC AGCCGACAGT 60  
 GATGAGATGG CCCCGGAGCC CCACAGCACA CCCACATCGA TGTGCACATC CACCAGGAGT 120  
 CTGCCCTGGC CAAGCTCCTG CTCACCTGCT GCTCTGCGCT GCGGCCCCGG GCCACCCAGG 180  
 25 CCAGGGGCG CAGCCGGCTG CTGGTGGCTT CGTGGGTGAT GCAGATCGTG CTGGGGATCT 240  
 TGAGTGCAGT CCTAGGAGGA TTTTCTTACA TCCGCGACTA CACCCTCCTC GTCACCTCGG 300  
 GAGCTGCCAT CTGGACAGGG GCTGTGGCTG TGCTGGCTGG AGCTGCTGCC TTCATTTAYG 360  
 30 AGAAACGGGG TGGTACATAC TGGGCCCTGC TGAGGACTCT GCTARCGCTG GCAGCTTTCT 420  
 CCACAGCCAT CGCTGCCCTC AAACCTTTGA ATGAAGATT CCGATATGGC TACTCTTATT 480  
 35 ACAACAGTGC CTGCCGCATC TCCAGCTCGA GTGACTGGAA CACTCCAGCC CCCACTCAGA 540  
 GTCCAGAAGA AGTCAGAAGG CTACACCTAT GTACCTCCTT CATGGACATG CTGAAGGCCT 600  
 TGTTCAGAAC CCTTCAGGCC ATGCTCTTGG GTGTCTGGAT TCTGCTGCTT CTGGCATCTC 660  
 40 TGGCCCTCT GTGGCTGTAC TGCTGGAGAA TGTTCCCAAC CAAAGGGAAA AGAGACCAGA 720  
 AGGAAATGTT GGAAGTGAGT GGAATCTAGC CATGCCTCTC CTGATTATTA GTGCCTGGTG 780  
 45 CTTCTGCACC GGGCGTCCCT GCATCTGACT GCTGGAAGAA GAACCAGACT GAGGAAAAGA 840  
 GGCTCTTCAA CAGCCCCAGT TATCCTGGCC CCATGACCGT GGCCACAGCC CTGCTCCAGC 900  
 AGCACTTGCC CATTCTTAC ACCCCTTCCC CATCCTGCTC CGCTTCATGT CCCCTCCTGA 960  
 50 GTAGTCATGT GATAATAAAC TCTCATGTTA TTGTTCCNAA AAAAAAAAAA AAAAAAAT 1020  
 TGGGGGGGGG CCGGTACCCA TTGGGCCTNN GGGGGNGGTT TAAATTAAT GGGGGGGGTT 1080  
 55 TAAAAGGG 1088

60 (2) INFORMATION FOR SEQ ID NO: 133:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 553 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

10 GGCAGAGAGC AGATGGCCTT GACACCAGCA GGGTGACATC CGCTATTGCT ACTTCTCTGC 60  
TCCCCACAG TTCCTCTGGA CTTCTCTGGA CCACAGTCCT CTGCCAGACC CCTGCCAGAC 120  
15 CCCAGTCCAC CATGATCCAT CTGGGTCACT TCCTCTTCCT GCTTTTGCTC CCAGTGGCTG 180  
CAGCTCAGAC GACTCCAGGA GAGAGATCAT CACTCCCTGC CTTTACCCCT GGCACCTTCAG 240  
GCTCTTGTTT CGGATGTGGG TCCCTCTCTC TGCGCTCCT GGCAGGCCTC GTGGCTGCTG 300  
20 ATGCGGTGGC ATCGCTGCTC ATCGTGGGGG CGGTGTTCTT GTGCGCACGC CCACGCCGCA 360  
GCCCCGCCCA AGATGGCAAA GTCTACATCA ACATGCCAGG CAGGGGCTGA CCCTCCTGCA 420  
GCTTGGACCT TTGACTTCTG ACCCTCTCAT CCTGGATGGT GTGTGGTGGC ACAGGAACCC 480  
25 CCGCCCCAAC TTTTGGATTG TAATAAAACA ATTGAAACAC CAAAAAAAAA AAAAAAAAAA 540  
AAAAAAAAAA AAA 553

30

## (2) INFORMATION FOR SEQ ID NO: 134:

35

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 467 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

40

Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu  
1 5 10 15

45

Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr  
20 25 30

Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala  
35 40 45

50

Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe  
50 55 60

55

Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys  
65 70 75 80

Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro  
85 90 95

60

Xaa Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe  
100 105 110

Asn Ala Asn Gln Trp Ala Xaa Ile Phe Gln Ala Ser Gly Ala Lys Tyr  
 115 120 125  
 5 Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser  
 130 135 140  
 Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp  
 145 150 155 160  
 10 Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg  
 165 170 175  
 Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu  
 180 185 190  
 15 Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys  
 195 200 205  
 20 Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val  
 210 215 220  
 Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Xaa  
 225 230 235 240  
 25 Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr  
 245 250 255  
 30 Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly  
 260 265 270  
 Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro  
 275 280 285  
 35 His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr  
 290 295 300  
 Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val  
 305 310 315 320  
 40 Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn  
 325 330 335  
 Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg  
 340 345 350  
 45 Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr  
 355 360 365  
 50 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val  
 370 375 380  
 Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu  
 385 390 395 400  
 55 Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile  
 405 410 415  
 60 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn  
 420 425 430

280

Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu  
 435 440 445

5 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr  
 450 455 460

Asn Val Ile  
 465

10

(2) INFORMATION FOR SEQ ID NO: 135:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 222 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

20 Met Trp Ser Ala Gly Arg Gly Gly Ala Ala Trp Pro Val Leu Leu Gly  
 1 5 10 15

25 Leu Leu Leu Ala Leu Leu Val Pro Gly Gly Gly Ala Ala Lys Thr Gly  
 20 25 30

Ala Glu Leu Val Thr Cys Gly Ser Val Leu Lys Leu Leu Asn Thr His  
 35 40 45

30 His Arg Val Arg Leu His Ser His Asp Ile Lys Tyr Gly Ser Gly Ser  
 50 55 60

Gly Gln Gln Ser Val Thr Gly Val Glu Ala Ser Asp Asp Ala Asn Ser  
 65 70 75 80

35 Tyr Trp Arg Ile Arg Gly Gly Ser Glu Gly Gly Cys Arg Arg Gly Ser  
 85 90 95

40 Pro Val Arg Cys Gly Gln Ala Val Arg Leu Thr His Val Leu Thr Gly  
 100 105 110

Lys Asn Leu His Thr His His Phe Pro Ser Pro Leu Ser Asn Asn Gln  
 115 120 125

45 Glu Val Ser Ala Phe Gly Glu Asp Gly Glu Gly Asp Asp Leu Asp Leu  
 130 135 140

Trp Thr Val Arg Cys Ser Gly Gln His Trp Glu Arg Glu Ala Ala Val  
 145 150 155 160

50 Arg Phe Gln His Val Gly Thr Ser Val Phe Leu Ser Val Thr Gly Glu  
 165 170 175

Gln Tyr Gly Ser Pro Ile Arg Gly Gln His Glu Val His Gly Met Pro  
 180 185 190

Ser Ala Asn Thr His Asn Thr Trp Lys Ala Met Glu Gly Ile Phe Ile  
 195 200 205

60 Lys Pro Ser Val Glu Pro Ser Ala Gly His Asp Glu Leu Xaa

281

210

215

220

## 5 (2) INFORMATION FOR SEQ ID NO: 136:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 156 amino acids

(B) TYPE: amino acid

10 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

Met Val Ile Glu Ile Ser Asn Lys Thr Ser Ser Ser Thr Cys Ile  
 1 5 10 15  
 Leu Val Leu Leu Val Ser Phe Cys Leu Leu Leu Val Pro Ala Met Tyr  
 20 25 30  
 Ser Ser Asp Thr Arg Gly Ser Leu Pro Ala Glu His Gly Val Leu Ser  
 35 40 45  
 Arg Gln Leu Arg Ala Leu Pro Ser Glu Asp Pro Tyr Gln Leu Glu Leu  
 50 55 60  
 Pro Ala Leu Gln Ser Glu Val Pro Lys Asp Ser Thr His Gln Trp Leu  
 65 70 75 80  
 Asp Gly Ser Asp Cys Val Leu Gln Ala Pro Gly Asn Thr Ser Cys Leu  
 85 90 95  
 Leu His Tyr Met Pro Gln Ala Pro Ser Ala Glu Pro Pro Leu Glu Trp  
 100 105 110  
 Pro Phe Pro Asp Leu Phe Ser Glu Pro Leu Cys Arg Gly Pro Ile Leu  
 115 120 125  
 Pro Leu Gln Ala Asn Leu Thr Arg Lys Gly Gly Trp Leu Pro Thr Gly  
 130 135 140  
 Ser Pro Ser Val Ile Leu Gln Asp Arg Tyr Ser Gly  
 145 150 155

## 45 (2) INFORMATION FOR SEQ ID NO: 137:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 233 amino acids

(B) TYPE: amino acid

50 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

Met Met Ile Leu Phe Asn Leu Leu Ile Phe Leu Cys Gly Ala Ala Leu  
 1 5 10 15  
 Leu Ala Val Gly Ile Trp Val Ser Ile Asp Gly Ala Ser Phe Leu Lys  
 20 25 30  
 Ile Phe Gly Pro Leu Ser Ser Ser Ala Met Gln Phe Val Asn Val Gly  
 35 40 45

282

Tyr Phe Leu Ile Ala Ala Gly Val Val Val Phe Ala Leu Gly Phe Leu  
 50 55 60  
 5 Gly Cys Tyr Gly Ala Lys Thr Glu Ser Lys Cys Ala Leu Val Thr Phe  
 65 70 75 80  
 Phe Phe Ile Leu Leu Leu Ile Phe Ile Ala Glu Val Ala Ala Val  
 85 90 95  
 10 Val Ala Leu Val Tyr Thr Thr Met Ala Glu His Phe Leu Thr Leu Leu  
 100 105 110  
 Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp Phe Thr  
 115 120 125  
 15 Gln Val Trp Asn Thr Thr Met Lys Gly Leu Lys Cys Cys Gly Phe Thr  
 130 135 140  
 20 Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu Asn Ser Ala  
 145 150 155 160  
 Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr Asn Thr Ala Asn Glu  
 165 170 175  
 25 Thr Cys Thr Lys Gln Lys Ala His Asp Gln Lys Val Glu Gly Cys Phe  
 180 185 190  
 30 Asn Gln Leu Leu Tyr Asp Ile Arg Thr Asn Ala Val Thr Val Gly Gly  
 195 200 205  
 Val Ala Ala Gly Ile Gly Gly Leu Glu Leu Ala Ala Met Ile Val Ser  
 210 215 220  
 35 Met Tyr Leu Tyr Cys Asn Leu Gln Xaa  
 225 230

40 (2) INFORMATION FOR SEQ ID NO: 138:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 61 amino acids

(B) TYPE: amino acid

45 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

Met Gly Ser Ser Arg Trp Ser Val Ala Cys Pro Thr Gly Leu Gly Val  
 1 5 10 15  
 50 Leu Met Leu Gly Leu Gly Gly Asp His Pro Pro Gly Ser Gln Val Asp  
 20 25 30  
 Pro Leu Leu Met Gly Xaa Cys Val Arg Pro Xaa Leu Pro Glu Leu Thr  
 35 40 45  
 55 Ala Xaa Trp Arg Glu Xaa Gln Xaa Arg Ser Ala Ser Ala  
 50 55 60  
 60



## (2) INFORMATION FOR SEQ ID NO: 139:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 73 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

10 Met Gly Trp Leu Phe Leu Lys Val Leu Leu Ala Gly Val Ser Phe Ser  
1 5 10 15  
Gly Phe Leu Tyr Pro Leu Val Asp Phe Cys Ile Ser Gly Lys Thr Arg  
20 25 30  
15 Gly Gln Lys Pro Asn Phe Val Ile Ile Leu Ala Asp Asp Met Gly Trp  
35 40 45  
20 Gly Asp Trp Gly Ala Asn Trp Ala Glu Thr Lys Asp Thr Ala Asn Leu  
50 55 60  
Asp Lys Met Ala Ser Glu Gly Met Xaa  
65 70

25

## (2) INFORMATION FOR SEQ ID NO: 140:

## (i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 377 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

35 Met His Gly Asn Glu Ala Leu Gly Arg Glu Leu Leu Leu Leu Met  
1 5 10 15  
Gln Phe Leu Cys His Glu Phe Leu Arg Gly Asn Pro Arg Val Thr Arg  
20 25 30  
40 Leu Leu Ser Glu Met Arg Ile His Leu Leu Pro Ser Met Asn Pro Asp  
35 40 45  
45 Gly Tyr Glu Ile Ala Tyr His Arg Gly Ser Glu Leu Val Gly Trp Ala  
50 55 60  
Glu Gly Arg Trp Asn Asn Gln Ser Ile Asp Leu Asn His Asn Phe Ala  
65 70 75 80  
50 Asp Leu Asn Thr Pro Leu Trp Glu Ala Gln Asp Asp Gly Lys Val Pro  
85 90 95  
His Ile Val Pro Asn His His Leu Pro Leu Pro Thr Tyr Tyr Thr Leu  
100 105 110  
55 Pro Asn Ala Thr Val Ala Pro Glu Thr Arg Ala Val Ile Lys Trp Met  
115 120 125  
60 Lys Arg Ile Pro Phe Val Leu Ser Ala Asn Leu His Gly Gly Glu Leu  
130 135 140

284

Val Val Ser Tyr Pro Phe Asp Met Thr Arg Thr Pro Trp Ala Ala Arg  
 145 150 155 160

5 Glu Leu Thr Pro Thr Pro Asp Asp Ala Val Phe Arg Trp Leu Ser Thr  
 165 170 175

Val Tyr Ala Gly Ser Asn Leu Ala Met Gln Asp Thr Ser Arg Arg Pro  
 180 185 190

10 Cys His Ser Gln Asp Phe Ser Val His Gly Asn Ile Ile Asn Gly Ala  
 195 200 205

Asp Trp His Thr Val Pro Gly Ser Met Asn Asp Phe Ser Tyr Leu His  
 210 215 220

15 Thr Asn Cys Phe Glu Val Thr Val Glu Leu Ser Cys Asp Lys Phe Pro  
 225 230 235 240

20 His Glu Asn Glu Leu Pro Gln Glu Trp Glu Asn Asn Lys Asp Ala Leu  
 245 250 255

Leu Thr Tyr Leu Glu Gln Val Arg Met Gly Ile Ala Gly Val Val Arg  
 260 265 270

25 Asp Lys Asp Thr Glu Leu Gly Ile Ala Asp Ala Val Ile Ala Val Asp  
 275 280 285

Gly Ile Asn His Asp Val Thr Thr Ala Trp Gly Gly Asp Tyr Trp Arg  
 290 295 300

30 Leu Leu Thr Pro Gly Asp Tyr Met Val Thr Ala Ser Ala Glu Gly Tyr  
 305 310 315 320

35 His Ser Val Thr Arg Asn Cys Arg Val Thr Phe Glu Glu Gly Pro Phe  
 325 330 335

Pro Cys Asn Phe Val Leu Thr Lys Thr Pro Lys Gln Arg Leu Arg Glu  
 340 345 350

40 Leu Leu Ala Ala Gly Ala Lys Val Pro Pro Asp Leu Arg Arg Arg Leu  
 355 360 365

Glu Arg Leu Arg Gly Gln Lys Asp Xaa  
 370 375

45

(2) INFORMATION FOR SEQ ID NO: 141:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 43 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

Met Ile Cys Leu Ile Leu Leu Leu Gln Ala Val Val Phe Leu Arg Ser  
 1 5 10 15

60

Leu His Val Val His Asn Phe Gln Ile Leu Asp Leu Ser Gly Thr Ser

285

20 25 30

Tyr Pro Lys Phe Tyr Gln Thr Leu His Arg Gln  
35 40

5

(2) INFORMATION FOR SEQ ID NO: 142:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 41 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

15  
Met Val His Val Leu Glu Ile Leu Leu Phe Ile Thr Met Gln Ala Val  
1 5 10 15  
Ser Phe Pro Phe Gln Thr Gln Ile Asp Thr Cys Asn Thr Gln Asp Pro  
20 20 25 30  
Ala Glu Arg Gln Pro Ala Ser Ile Val  
35 40

25

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 70 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

30  
Met Gly Ser Cys Ser Lys Asn Arg Ser Phe Phe Trp Met Thr Gly Leu  
1 5 10 15  
Leu Val Phe Ile Ser Leu Leu Leu Ser Glu Trp Gln Gly Pro Trp Glu  
40 20 25 30  
Gly Arg Ala Ile Gly Glu Gly Trp Ala Ser Trp Ala Leu Thr Asn Gly  
35 40 45  
Trp Ala Val Gln Leu Leu Met Ser Leu Gly Asn Asn Thr Glu Lys His  
45 50 55 60  
Ser Val Met Ile Tyr Glu  
65 70

50

(2) INFORMATION FOR SEQ ID NO: 144:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 483 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

55  
Met Ala Thr Gly Gly Gly Ile Arg Ala Met Thr Ser Leu Tyr Gly Glu

60

286

	1	5	10	15
	Leu Ala Gly	Leu Lys Glu Leu Gly	Leu Leu Asp Cys Xaa	Ser Tyr Ile
		20	25	30
5	Thr Gly Ala	Ser Gly Ser Thr Trp	Ala Leu Ala Asn Leu	Tyr Lys Asp
	35		40	45
	Pro Glu Trp	Ser Gln Lys Asp	Leu Ala Gly Pro Thr	Glu Leu Leu Lys
10	50	55	60	
	Thr Gln Val	Thr Lys Asn Lys Leu Gly	Val Leu Ala Pro Ser	Gln Leu
	65	70	75	80
15	Gln Arg Tyr	Arg Gln Glu Leu Ala	Glu Arg Ala Arg Leu	Gly Tyr Pro
		85	90	95
	Ser Cys Phe	Thr Asn Leu Trp Ala	Leu Ile Asn Glu Ala	Leu Leu His
		100	105	110
20	Asp Glu Pro	His Asp His Lys Leu Ser	Asp Gln Arg Glu Ala	Leu Ser
	115	120	125	
	His Gly Gln	Asn Pro Leu Pro Ile Tyr	Cys Ala Leu Asn Thr	Lys Gly
25	130	135	140	
	Gln Ser Leu	Thr Thr Phe Glu Phe Gly	Glu Trp Cys Glu Phe	Ser Pro
	145	150	155	160
30	Tyr Glu Val	Gly Phe Pro Lys Tyr Gly	Ala Phe Ile Pro Ser	Glu Leu
		165	170	175
	Phe Gly Ser	Glu Phe Phe Met Gly Gln	Leu Met Lys Arg Leu	Pro Glu
		180	185	190
35	Ser Arg Ile	Cys Phe Leu Glu Gly Ile	Trp Ser Asn Leu Tyr	Ala Ala
	195	200	205	
	Asn Leu Gln	Asp Ser Leu Tyr Trp Ala	Ser Glu Pro Ser Gln	Phe Trp
40	210	215	220	
	Asp Arg Trp	Val Arg Asn Gln Ala Asn	Leu Asp Lys Glu Gln	Val Pro
	225	230	235	240
45	Leu Leu Lys	Ile Glu Glu Pro Pro Ser	Thr Ala Gly Arg Ile	Ala Glu
		245	250	255
	Phe Phe Thr	Asp Leu Leu Thr Trp Arg	Pro Leu Ala Gln Ala	Thr His
		260	265	270
50	Asn Phe Leu	Arg Gly Leu His Phe His	Lys Asp Tyr Phe Gln	His Pro
	275	280	285	
	His Phe Ser	Thr Trp Lys Ala Thr Thr	Leu Asp Gly Leu Pro	Asn Gln
55	290	295	300	
	Leu Thr Pro	Ser Glu Pro His Leu Cys	Leu Leu Asp Val Gly	Tyr Leu
	305	310	315	320
60	Ile Asn Thr	Ser Cys Leu Pro Leu Leu	Gln Pro Thr Arg Asp	Val Asp

287

[illegible]

35 (2) INFORMATION FOR SEQ ID NO: 145:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 226 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

[illegible]

288

Asn Leu Glu Asn Leu Glu Glu Lys Glu Tyr Phe Gly Ile Val Ser Val  
 100 105 110  
 5 Arg Ile Leu Val His Glu Trp Pro Met Thr Ser Gly Ser Ser Leu Gln  
 115 120 125  
 Leu Ile Val Ile Gln Glu Glu Val Val Glu Ile Asp Gly Lys Gln Val  
 130 135 140  
 10 Gln Gln Lys Asp Val Thr Glu Ile Asp Ile Leu Val Lys Asn Arg Gly  
 145 150 155 160  
 Val Leu Arg His Ser Asn Tyr Thr Leu Pro Leu Glu Glu Ser Met Leu  
 165 170 175  
 15 Tyr Ser Ile Ser Arg Asp Ser Asp Ile Leu Phe Thr Leu Pro Asn Leu  
 180 185 190  
 Ser Lys Lys Glu Ser Val Ser Ser Leu Gln Thr Thr Ser Gln Tyr Leu  
 195 200 205  
 20 Ile Arg Asn Val Glu Thr Thr Val Asp Glu Asp Val Leu Pro Gly Gln  
 210 215 220  
 25 Val Thr  
 225

30 (2) INFORMATION FOR SEQ ID NO: 146:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 45 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

Met Gly Met Gly Ala Phe Gln Ala Phe Phe Trp Val Ile Leu Thr Val  
 1 5 10 15  
 40 Ser Asn Val Cys Val Leu Phe Lys Met Ser Leu Phe Phe Leu Leu Thr  
 20 25 30  
 45 Leu Ile Ser Lys Leu His Gly Asp Ala Glu Val Cys Xaa  
 35 40 45

50 (2) INFORMATION FOR SEQ ID NO: 147:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 132 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

Met Ser Gly Gly Trp Met Ala Gln Val Gly Ala Trp Arg Thr Gly Ala  
 1 5 10 15  
 60 Leu Gly Leu Ala Leu Leu Leu Leu Gly Leu Gly Leu Gly Leu Glu

289

20 25 30

Ala Pro Arg Ala Arg Phe Pro Pro Arg Pro Leu Pro Arg Pro His Pro  
35 40 45

5 Ser Ser Gly Ser Cys Pro Pro Thr Lys Phe Gln Cys Arg Thr Ser Gly  
50 55 60

10 Leu Cys Val Pro Leu Thr Trp Arg Cys Asp Arg Thr Trp Thr Ala Ala  
65 70 75 80

Met Ala Ala Met Arg Arg Ser Ala Gly Leu Ser His Val Pro Arg Lys  
85 90 95

15 Gly Asn Ala His Arg Pro Leu Ala Ser Pro Ala Pro Ala Pro Ala Ser  
100 105 110

Val Thr Ala Leu Gly Glu Leu Thr Arg Asn Cys Ala Thr Ala Ala Ala  
115 120 125

20 Trp Pro Ala Xaa  
130

25

(2) INFORMATION FOR SEQ ID NO: 148:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 92 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

35 Met Glu Ala Thr Leu Glu Gln His Leu Glu Asp Thr Met Lys Asn Pro  
1 5 10 15

Ser Ile Val Gly Val Leu Cys Thr Asp Ser Gln Gly Leu Asn Leu Gly  
20 25 30

40 Cys Arg Gly Thr Leu Ser Asp Glu His Ala Gly Val Ile Ser Val Leu  
35 40 45

Ala Gln Gln Ala Ala Lys Leu Thr Ser Asp Pro Thr Asp Ile Pro Val  
50 55 60

45 Val Cys Leu Glu Ser Asp Asn Gly Asn Ile Met Ile Gln Lys His Asp  
65 70 75 80

50 Gly Ile Thr Val Ala Val His Lys Met Ala Ser Xaa  
85 90

55 (2) INFORMATION FOR SEQ ID NO: 149:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 165 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

290

Met Glu Pro Leu Arg Leu Leu Ile Leu Leu Phe Val Thr Glu Leu Ser  
 1 5 10 15

5 Gly Ala His Asn Thr Thr Val Phe Gln Gly Val Ala Gly Gln Ser Leu  
 20 25 30

Gln Val Ser Cys Pro Tyr Asp Ser Met Lys His Trp Gly Arg Arg Lys  
 35 40 45

10 Ala Trp Cys Arg Gln Leu Gly Glu Lys Gly Pro Cys Gln Arg Val Val  
 50 55 60

15 Ser Thr His Asn Leu Trp Leu Leu Ser Phe Leu Arg Arg Trp Asn Gly  
 65 70 75 80

Ser Thr Ala Ile Thr Asp Asp Thr Leu Gly Gly Thr Leu Thr Ile Thr  
 85 90 95

20 Leu Arg Asn Leu Gln Pro His Asp Ala Gly Leu Tyr Gln Cys Gln Ser  
 100 105 110

Leu His Gly Ser Glu Ala Asp Thr Leu Arg Lys Val Leu Val Glu Val  
 115 120 125

25 Leu Ala Asp Pro Leu Asp His Arg Asp Ala Gly Asp Leu Trp Phe Pro  
 130 135 140

30 Gly Glu Ser Glu Ser Phe Glu Asp Ala His Val Glu His Ser Ile Ser  
 145 150 155 160

Arg Ser Ser Ser Xaa  
 165

35

(2) INFORMATION FOR SEQ ID NO: 150:

- (i) SEQUENCE CHARACTERISTICS:
- 40 (A) LENGTH: 139 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

45 Met Ile Ser Leu Thr Asp Thr Gln Lys Ile Gly Met Gly Leu Thr Gly  
 1 5 10 15

Phe Gly Val Phe Phe Leu Phe Phe Gly Met Ile Leu Phe Phe Asp Lys  
 20 25 30

50 Ala Leu Leu Ala Ile Gly Asn Val Leu Phe Val Ala Gly Leu Ala Phe  
 35 40 45

55 Val Ile Gly Leu Glu Arg Thr Phe Arg Phe Phe Phe Gln Lys His Lys  
 50 55 60

Met Lys Ala Thr Gly Phe Phe Leu Gly Gly Val Phe Val Val Leu Ile  
 65 70 75 80

60 Gly Trp Pro Leu Ile Gly Met Ile Phe Glu Ile Tyr Gly Phe Phe Leu



.291

85 90 95

Leu Phe Arg Gly Phe Phe Pro Val Val Val Gly Phe Ile Arg Arg Val  
100 105 110

5 Pro Val Leu Gly Ser Leu Leu Asn Leu Pro Gly Ile Arg Ser Phe Val  
115 120 125

10 Asp Lys Val Gly Glu Ser Asn Asn Met Val Xaa  
130 135

15 (2) INFORMATION FOR SEQ ID NO: 151:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 58 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

Met Ser Ala Pro Gln Thr Arg Ile Ser Arg Ala Leu Val Leu Leu Phe  
1 5 10 15

25 Leu Ala Pro Thr Leu Leu Ser Leu Gly His Gly Ile His Pro Ile Asn  
20 25 30

Thr Ala Thr Pro Tyr Xaa Thr Asp Gln Ala Lys Leu Ala Pro Gly Thr  
35 40 45

30 Lys Glu Leu Asn His Asp Gln Ser Val Thr  
50 55

35

(2) INFORMATION FOR SEQ ID NO: 152:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 48 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

Met Ile Arg Lys Leu His Lys Ile Ile Val Phe Ser Pro Arg Val Ile  
45 1 5 10 15

Val Leu Leu Asn Cys Phe Phe Phe Ile Lys Ala Lys Phe Val Leu Tyr  
20 25 30

50 Ile Phe Val Phe His Val Leu Asp Gly Ser Ile Ser Tyr Pro Val Xaa  
35 40 45

55

(2) INFORMATION FOR SEQ ID NO: 153:

60

(i) SEQUENCE CHARACTERISTICS:

292

(A) LENGTH: 42 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

5

Met Leu Leu Asn Gln His Phe Lys Ile Phe Gly Ser Leu Ile His Met  
 1 5 10 15

10

Asn Leu Leu Phe Ala Leu Ile Ser Leu Gly Ser Ser Asn Leu Ser Gly  
 20 25 30

Val Gln Phe Cys Cys Glu Thr Val Gln Xaa  
 35 40

15

(2) INFORMATION FOR SEQ ID NO: 154:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 72 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

25

Met Leu Ser Leu Ser Phe Leu Leu Arg Arg Val Leu Phe Leu Gly Phe  
 1 5 10 15

Leu Gln Ala Ser Val Gly Glu Lys Lys Ser Leu Arg Xaa Leu Asn Tyr  
 20 25 30

30

Ser Val Pro His Pro Met Leu Xaa His Pro Pro Pro Asp Thr Ala Gln  
 35 40 45

35

Val Pro Pro Arg Leu Glu Arg Ser Leu Leu Gln Gln Glu Leu Trp Thr  
 50 55 60

Pro Gly Pro His His Ser Asn Ile  
 65 70

40

(2) INFORMATION FOR SEQ ID NO: 155:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 106 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

50

Met Gln Pro Leu Asn Phe Ser Ser Thr Glu Cys Ser Ser Phe Ser Pro  
 1 5 10 15

Pro Thr Thr Val Ile Leu Leu Ile Leu Leu Cys Phe Glu Gly Leu Leu  
 20 25 30

55

Phe Leu Ile Phe Thr Ser Val Met Phe Gly Thr Gln Val His Ser Ile  
 35 40 45

60

Cys Thr Asp Glu Thr Gly Ile Glu Gln Leu Lys Lys Glu Glu Arg Arg  
 50 55 60

Trp Ala Lys Lys Thr Lys Trp Met Asn Met Lys Ala Val Phe Gly His  
 65 70 75 80

5 Pro Phe Ser Leu Gly Trp Ala Ser Pro Phe Ala Thr Pro Asp Gln Gly  
 85 90 95

Lys Ala Asp Pro Tyr Gln Tyr Val Val Xaa  
 100 105

10

## (2) INFORMATION FOR SEQ ID NO: 156:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 29 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

20 Met Tyr Thr Asn His Phe Asn Leu Tyr Leu Lys Tyr Ile Leu Leu Ile  
 1 5 10 15

25 Ile Leu Ile Leu Asn Met Thr Asn Ser Ser Ser Arg Tyr  
 20 25

## (2) INFORMATION FOR SEQ ID NO: 157:

30 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 53 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

35 Met Asn Glu Leu Leu Leu Phe Phe Phe Phe Phe Phe Phe Thr Phe  
 1 5 10 15

40 Cys Ile Glu Thr Asn Ser Phe Lys Gln Thr Tyr Tyr Tyr Tyr Phe Leu  
 20 25 30

Gln Asn Ile Tyr Met Glu Met Leu Pro Pro Pro Val Asn Pro Pro Val  
 35 40 45

45 Pro Pro Trp Gly Xaa  
 50

50 (2) INFORMATION FOR SEQ ID NO: 158:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 75 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

55 Met Tyr Ala Val Tyr Gln Gln Leu Ala Gln Leu Thr Leu Met Val Thr  
 1 5 10 15

60

294

Leu Leu Ala Pro Ile Leu Pro Asp Glu Gln Ser Glu Val Phe Glu Ala  
                   20                  25                  30

5 Leu Ser Asn Leu Pro Lys Val Thr Trp Leu Gly Ser Asn Ser Pro Ser  
                   35                  40                  45

Ser Glu Met Pro Glu Pro Gly Arg Phe Val Ile Val His His Gln Leu  
           50                  55                  60

10 Ser Ala Ala Ser His Ser Ser Ser Gln Leu Ala  
       65                  70                  75

15

(2) INFORMATION FOR SEQ ID NO: 159:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 81 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

25 Met Trp Pro Pro Leu Leu Leu Leu Leu Leu Leu Pro Ala Ala Pro  
       1                  5                  10                  15

Val Pro Thr Ala Lys Ala Ala Pro His Pro Asp Ala Asn Thr Gln Glu  
                   20                  25                  30

30 Gly Leu Gln Asn Leu Leu Gln Gly Val Gly Ala Gly Gly Asp Gly Glu  
           35                  40                  45

Leu Arg Ala Asp Ser His Leu Ala Pro Gly Ser Gly Cys Ile Asp Gly  
       50                  55                  60

35 Ala Val Val Ala Thr Arg Pro Glu Ser Arg Gly Gly Arg Pro Ala Val  
       65                  70                  75                  80

40 Pro

40

(2) INFORMATION FOR SEQ ID NO: 160:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 139 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

50

Met Lys Phe Thr Thr Leu Leu Phe Leu Ala Ala Val Ala Gly Ala Leu  
       1                  5                  10                  15

55 Val Tyr Ala Glu Asp Ala Ser Ser Asp Ser Thr Gly Ala Asp Pro Ala  
           20                  25                  30

Gln Glu Ala Gly Thr Ser Lys Pro Asn Glu Glu Ile Ser Gly Pro Ala  
       35                  40                  45

60

295

Glu Pro Ala Ser Pro Pro Glu Thr Thr Thr Thr Ala Gln Glu Thr Ser  
 50 55 60

5 Ala Ala Ala Val Gln Gly Thr Ala Lys Val Thr Ser Ser Arg Gln Glu  
 65 70 75 80

Leu Asn Pro Leu Lys Ser Ile Val Glu Lys Ser Ile Leu Leu Thr Glu  
 85 90 95

10 Gln Ala Leu Ala Lys Ala Gly Lys Gly Met His Gly Gly Val Pro Gly  
 100 105 110

Gly Lys Gln Phe Ile Glu Asn Gly Ser Glu Phe Ala Gln Lys Leu Leu  
 115 120 125

15 Lys Lys Phe Ser Leu Leu Lys Pro Trp Ala Xaa  
 130 135

20 (2) INFORMATION FOR SEQ ID NO: 161:  
 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 178 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

25 Met Leu Gly Cys Gly Ile Pro Ala Leu Gly Leu Leu Leu Leu Gln  
 1 5 10 15

Gly Ser Ala Asp Gly Asn Gly Ile Gln Gly Phe Phe Tyr Pro Trp Ser  
 20 25 30

35 Cys Glu Gly Asp Ile Trp Asp Arg Glu Ser Cys Gly Gly Gln Ala Ala  
 35 40 45

Ile Asp Ser Pro Asn Leu Cys Leu Arg Leu Arg Cys Cys Tyr Arg Asn  
 50 55 60

40 Gly Val Cys Tyr His Gln Arg Pro Asp Glu Asn Val Arg Arg Lys His  
 65 70 75 80

45 Met Trp Ala Leu Val Trp Thr Cys Ser Gly Leu Leu Leu Leu Ser Cys  
 85 90 95

Ser Ile Cys Leu Phe Trp Trp Ala Lys Arg Arg Asp Val Leu His Met  
 100 105 110

50 Pro Gly Phe Leu Ala Gly Pro Cys Asp Met Ser Lys Ser Val Ser Leu  
 115 120 125

Leu Ser Lys His Arg Gly Thr Lys Lys Thr Pro Ser Thr Gly Ser Val  
 130 135 140

55 Pro Val Ala Leu Ser Lys Glu Ser Arg Asp Val Glu Gly Gly Thr Glu  
 145 150 155 160

60 Gly Glu Gly Thr Glu Glu Gly Glu Glu Thr Glu Gly Glu Glu Glu  
 165 170 175

Asp Xaa

5

(2) INFORMATION FOR SEQ ID NO: 162:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 72 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

15

Met Glu Ala Val Phe Thr Val Phe Phe Phe Val Val Val Leu Phe Leu  
1 5 10 15Lys Asn Thr Glu Gly Ala Lys Leu Phe Cys Thr Leu Tyr Pro Ala Ala  
20 25 30

20

Ser Ser Gly Gln Ser Gln Gly Pro Gly Leu Glu Lys Pro Asp Ser Gln  
35 40 45

25

Glu Cys Ile Ile Asp Pro Cys Ser Tyr Pro Ile Ala Leu Gly Ala Gly  
50 55 60Thr Glu Pro Gly Cys Lys Ile Xaa  
65 70

30

(2) INFORMATION FOR SEQ ID NO: 163:

(i) SEQUENCE CHARACTERISTICS:

35

(A) LENGTH: 67 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

40

Met Trp Phe Tyr Phe Leu Ser Val Ser Phe Pro Leu Leu Pro Val Xaa  
1 5 10 15Ala Pro Xaa Pro Pro Pro Ala Pro Thr Thr Leu Cys Leu Leu Leu Phe  
20 25 30

45

Leu Gly Xaa Leu Tyr Asn Ser Thr Cys Ile His Cys Val His Thr Thr  
35 40 45

50

Ser Xaa Thr Gln Asn Pro Thr Ala Asn Thr Leu Lys Lys Lys Lys  
50 55 60Asn Trp Gly  
65

55

(2) INFORMATION FOR SEQ ID NO: 164:

(i) SEQUENCE CHARACTERISTICS:

60

(A) LENGTH: 155 amino acids

297

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

5 Met Gly Phe Gly Ala Thr Leu Ala Val Gly Leu Thr Ile Phe Val Leu  
1 5 10 15

Ser Val Val Thr Ile Ile Ile Cys Phe Thr Cys Ser Cys Cys Cys Leu  
20 25 30

10 Tyr Lys Thr Cys Arg Arg Pro Arg Pro Val Val Thr Thr Thr Thr Ser  
35 40 45

Thr Thr Val Val His Ala Pro Tyr Pro Gln Pro Pro Ser Val Pro Pro  
15 50 55 60

Ser Tyr Pro Gly Pro Ser Tyr Gln Gly Tyr His Thr Met Pro Pro Gln  
65 70 75 80

20 Pro Gly Met Pro Ala Ala Pro Tyr Pro Met Gln Tyr Pro Pro Pro Tyr  
85 90 95

Pro Ala Gln Pro Met Gly Pro Pro Ala Tyr His Glu Thr Leu Ala Gly  
100 105 110

25 Glu Gln Pro Arg Pro Thr Pro Pro Ala Ser Leu Leu Thr Thr Arg Pro  
115 120 125

Thr Trp Met Pro Arg Arg Arg Pro Ser Glu His Ser Leu Ala Ser Leu  
130 135 140

Ala Ala Thr Trp Leu Cys Cys Val Cys Ala Xaa  
145 150 155

35

(2) INFORMATION FOR SEQ ID NO: 165:

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 104 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

45 Met Ile Ile Leu Val Phe Ile Ala Phe Phe Ile Pro Leu Gln Lys Thr  
1 5 10 15

Ile Gly Lys Ile Ala Thr Cys Leu Glu Leu Arg Ser Ala Ala Leu Gln  
20 25 30

50 Ser Thr Gln Ser Gln Glu Glu Phe Lys Leu Glu Asp Leu Lys Lys Leu  
35 40 45

Glu Pro Ile Leu Lys Asn Ile Leu Thr Tyr Asn Lys Glu Phe Pro Phe  
55 60

Asp Val Gln Pro Val Pro Leu Arg Arg Ile Leu Ala Pro Gly Glu Glu  
65 70 75 80

60 Glu Asn Leu Glu Phe Glu Glu Asp Glu Glu Glu Gly Gly Ala Gly Ala

298

85

90

95

Gly Leu Leu Ile Leu Ser Cys Xaa  
100

5

(2) INFORMATION FOR SEQ ID NO: 166:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 81 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

15

Met Ala Gly Thr Met Val Ile Val Val Val Val Val Gly Glu Val  
1 5 10 15

20

Val Val Glu Ala Glu Val Val Val Gln Ala Arg Glu Glu Ala Gly Glu  
20 25 30

Glu Glu Gly Ala Arg Ile Ile Thr Lys Gly Val Asn Leu Asn Ser Ile  
35 40 45

25

Ser Ser Met Glu Val Ile Ser Ile Ile Ile Leu Asp Leu Asp Arg Glu  
50 55 60

30

Asp Ile Thr Leu Val Glu Ala Thr Glu Pro Tyr Ile Leu Leu Glu Leu  
65 70 75 80

Lys

35

(2) INFORMATION FOR SEQ ID NO: 167:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 93 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

40

Met Ser Phe Ser Phe Ile Ile Phe Leu Leu Leu Val Cys Gln Glu Ile  
1 5 10 15

45

Thr Phe Cys Met Ser Tyr Gly Asp Ala Val Asn Cys Phe Ser Glu Cys  
20 25 30

50

Phe Ser Asn Leu Gln Thr Ile Tyr Ile Ser Cys Leu Gln His Ala Val  
35 40 45

Cys Lys His Ser Val Ile Trp Ser Ile Gln Leu Phe Val Arg Ala Leu  
50 55 60

55

Pro Ile Ser Lys Cys Ala Glu Leu Ser Ile Asp Gly Ile Phe Arg Ser  
65 70 75 80

60

Phe His Glu Asn Trp Lys Cys Ser Trp Val Ala Pro Thr  
85 90



5 (2) INFORMATION FOR SEQ ID NO: 168:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 58 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

Met Gly Trp Ser Ala Gly Leu Leu Phe Leu Leu Ile Leu Tyr Leu Pro  
 1 5 10 15  
 Val Pro Gly Trp Met Glu Arg Glu Asp Gly Glu Thr Gly His Leu Ser  
 20 25 30  
 Pro Gln Ala Pro Gly Arg Glu Tyr Arg Gly Phe Tyr Ser Val Pro Pro  
 35 40 45  
 Asp Tyr Val Trp Leu Arg Asp Ser Pro Xaa  
 50 55

25 (2) INFORMATION FOR SEQ ID NO: 169:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 232 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

35 Met Ala Thr Leu Trp Gly Gly Leu Leu Arg Leu Gly Ser Leu Leu Ser  
 1 5 10 15  
 Leu Ser Cys Leu Ala Leu Ser Val Leu Leu Leu Ala His Cys Gln Thr  
 20 25 30  
 40 Pro Pro Arg Ile Ser Arg Met Ser Asp Val Asn Val Ser Ala Leu Pro  
 35 40 45  
 Ile Lys Lys Asn Ser Gly His Ile Tyr Asn Lys Asn Ile Ser Gln Lys  
 50 55 60  
 45 Asp Cys Asp Cys Leu His Val Val Glu Pro Met Pro Val Arg Gly Pro  
 65 70 75 80  
 Asp Val Glu Ala Tyr Cys Leu Arg Cys Glu Cys Lys Tyr Glu Glu Arg  
 50 85 90 95  
 Ser Ser Val Thr Ile Lys Val Thr Ile Ile Ile Tyr Leu Ser Ile Leu  
 100 105 110  
 55 Gly Leu Leu Leu Leu Tyr Met Val Tyr Leu Thr Leu Val Glu Pro Ile  
 115 120 125  
 Leu Lys Arg Arg Leu Phe Gly His Ala Gln Leu Ile Gln Ser Asp Asp  
 130 135 140  
 60

300

Asp Ile Gly Asp His Gln Pro Phe Ala Asn Ala His Asp Val Leu Ala  
 145 150 155 160  
 5 Arg Ser Arg Ser Arg Ala Asn Val Leu Asn Lys Val Glu Tyr Gly Thr  
 165 170 175  
 Ala Ala Leu Glu Ala Ser Ser Pro Arg Ala Ala Lys Ser Leu Ser Leu  
 180 185 190  
 10 Thr Gly Met Leu Ser Ser Ala Asn Trp Gly Ile Glu Phe Lys Val Thr  
 195 200 205  
 Arg Lys Lys Gln Ala Asp Asn Trp Lys Gly Thr Asp Trp Val Leu Leu  
 210 215 220  
 15 Gly Phe Ile Leu Ile Pro Cys Xaa  
 225 230

20

(2) INFORMATION FOR SEQ ID NO: 170:

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 72 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

30 Met Ser Ala Ile Phe Asn Phe Gln Ser Leu Leu Thr Val Ile Leu Leu  
 1 5 10 15  
 Leu Ile Cys Thr Cys Ala Tyr Ile Arg Ser Leu Ala Pro Ser Leu Leu  
 20 25 30  
 35 Asp Arg Asn Lys Thr Gly Leu Leu Gly Ile Phe Trp Lys Cys Ala Arg  
 35 40 45  
 Ile Gly Glu Arg Lys Ser Pro Tyr Val Ala Val Cys Cys Ile Val Met  
 50 55 60  
 40 Ala Phe Ser Ile Leu Phe Ile Gln  
 65 70

45

(2) INFORMATION FOR SEQ ID NO: 171:

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH: 65 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

55 Met Gly Thr Phe Ser Leu Ser Leu Phe Gly Leu Met Gly Val Ala Phe  
 1 5 10 15  
 Gly Met Asn Leu Glu Ser Ser Leu Glu Glu Asp His Arg Ile Phe Trp  
 20 25 30  
 60 Leu Ile Thr Gly Ile Met Phe Met Gly Ser Gly Leu Ile Trp Arg Arg

35 40 45

Leu Leu Ser Phe Leu Gly Arg Gln Leu Glu Ala Pro Leu Pro Pro Met  
50 55 60

5

Val  
65

10

(2) INFORMATION FOR SEQ ID NO: 172:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 75 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

20

Met Tyr Lys Gly Lys Leu Val Ile Val Leu Ile Leu Leu Leu Leu Pro  
1 5 10 15

Ser His Phe Met Phe Leu Thr Gln Cys Lys Glu Ile Lys His Asn Leu  
20 25 30

25

Lys Lys Asn Met Ser Leu Leu Leu Phe Thr Ile Lys Ser Trp Leu Tyr  
35 40 45

Ser Ala Ser Leu Gly Ile Leu Tyr Asn Trp Gln His Leu Thr Ala Gln  
50 55 60

30

Val Asp Gln Cys Thr Ser Leu Ile Leu Ile His  
65 70 75

35

(2) INFORMATION FOR SEQ ID NO: 173:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 334 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:

45

Met Val Gly His Glu Met Ala Ser Xaa Ser Ser Asn Thr Ser Leu Pro  
1 5 10 15

Phe Ser Asn Met Gly Asn Pro Met Asn Thr Thr Gln Leu Gly Lys Ser  
20 25 30

50

Leu Phe Gln Trp Gln Val Glu Gln Glu Glu Ser Lys Leu Ala Asn Ile  
35 40 45

Ser Gln Asp Gln Phe Leu Ser Lys Asp Ala Asp Gly Asp Thr Phe Leu  
50 55 60

55

His Ile Ala Val Ala Gln Gly Arg Arg Ala Leu Ser Tyr Val Leu Ala  
65 70 75 80

Arg Lys Met Asn Ala Leu His Met Leu Asp Ile Lys Glu His Asn Gly  
85 90 95

60

302

Gln Ser Ala Phe Gln Val Ala Val Ala Ala Asn Gln His Leu Ile Val  
 100 105 110

5 Gln Asp Leu Val Asn Ile Gly Ala Gln Val Asn Thr Thr Asp Cys Trp  
 115 120 125

Gly Arg Thr Pro Leu His Val Cys Ala Glu Lys Gly His Ser Gln Val  
 130 135 140

10 Leu Gln Ala Ile Gln Lys Gly Ala Val Gly Ser Asn Gln Phe Val Asp  
 145 150 155 160

15 Leu Glu Ala Thr Asn Tyr Asp Gly Leu Thr Pro Leu His Cys Ala Val  
 165 170 175

Ile Ala His Asn Ala Val Val His Glu Leu Gln Arg Asn Gln Gln Pro  
 180 185 190

20 His Ser Pro Glu Val Gln Glu Leu Leu Lys Asn Lys Ser Leu Val  
 195 200 205

Asp Thr Ile Lys Cys Leu Ile Gln Met Gly Ala Ala Val Glu Ala Lys  
 210 215 220

25 Asp Arg Lys Ser Gly Arg Thr Ala Leu His Leu Ala Ala Glu Glu Ala  
 225 230 235 240

30 Asn Leu Glu Leu Ile Arg Leu Phe Leu Glu Leu Pro Ser Cys Leu Ser  
 245 250 255

Phe Val Asn Ala Lys Ala Tyr Asn Gly Asn Thr Ala Leu His Val Ala  
 260 265 270

35 Ala Ser Leu Gln Tyr Arg Leu Thr Gln Leu Asp Ala Val Arg Leu Leu  
 275 280 285

Met Arg Lys Gly Ala Asp Pro Ser Thr Arg Asn Leu Glu Asn Glu Gln  
 290 295 300

40 Pro Val His Leu Val Pro Asp Gly Pro Val Gly Glu Gln Ile Arg Arg  
 305 310 315 320

45 Ile Leu Lys Gly Lys Ser Ile Gln Gln Arg Ala Pro Pro Tyr  
 325 330

(2) INFORMATION FOR SEQ ID NO: 174:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 196 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

Met Asp Ala Arg Trp Trp Ala Val Val Val Leu Ala Ala Phe Pro Ser  
 1 5 10 15

60

Leu Gly Ala Gly Gly Glu Thr Pro Glu Ala Pro Pro Glu Ser Trp Thr

303

	20	25	30
	Gln Leu Trp Phe Phe Arg Phe Val Val Asn Ala Ala Gly Tyr Ala Ser		
	35	40	45
5	Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Phe Arg Arg Lys Asn		
	50	55	60
10	Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys		
	65	70	75
	Val Phe Gly Asn Glu Pro Lys Ala Ser Asp Glu Val Pro Leu Ala Pro		
	85	90	95
15	Arg Thr Glu Ala Ala Glu Thr Thr Pro Met Trp Gln Ala Leu Lys Leu		
	100	105	110
	Leu Phe Cys Ala Thr Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Val		
	115	120	125
20	Leu Gln Glu Arg Val Met Thr Arg Ser Tyr Gly Ala Thr Ala Thr Ser		
	130	135	140
25	Pro Gly Glu Arg Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg		
	145	150	155
	Val Leu Ala Leu Ile Val Ala Gly Leu Ser Cys Val Leu Cys Lys Gln		
	165	170	175
30	Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Cys Gln Pro Val		
	180	185	190
	Gln Cys Ala Xaa		
	195		

35

(2) INFORMATION FOR SEQ ID NO: 175:

40

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 265 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 175:

45

Met	Ser	Asp	Leu	Leu	Leu	Leu	Gly	Leu	Ile	Gly	Gly	Leu	Thr	Leu	Leu
1				5					10					15	

50

Leu	Leu	Leu	Thr	Leu	Leu	Ala	Phe	Ala	Gly	Tyr	Ser	Gly	Leu	Leu	Ala
			20					25					30		

Gly	Val	Glu	Val	Ser	Ala	Gly	Ser	Pro	Pro	Ile	Arg	Asn	Val	Thr	Val
		35					40					45			

55

Ala	Tyr	Lys	Phe	His	Met	Gly	Leu	Tyr	Gly	Glu	Thr	Gly	Arg	Leu	Phe
	50					55				60					

Thr	Glu	Ser	Cys	Ser	Ile	Ser	Pro	Lys	Leu	Arg	Ser	Ile	Ala	Val	Tyr
65					70					75				80	

60

304

Tyr Asp Asn Pro His Met Val Pro Pro Asp Lys Cys Arg Cys Ala Val  
 85 90 95  
 5 Gly Ser Ile Leu Ser Glu Gly Glu Glu Ser Pro Ser Pro Glu Leu Ile  
 100 105 110  
 Asp Leu Tyr Gln Lys Phe Gly Phe Lys Val Phe Ser Phe Pro Glu Pro  
 115 120 125  
 10 Ser His Val Val Thr Ala Thr Phe Pro Leu Thr Pro Pro Phe Cys Pro  
 130 135 140  
 Ile Trp Leu Gly Tyr Pro Pro Cys Pro Ser Cys Leu Gly His Leu His  
 145 150 155 160  
 15 Gln Gly Ala Glu Ala Val Cys Leu Ser Ser Ala Gly Asp Leu Pro Gly  
 165 170 175  
 Arg Pro Glu Ser Ile Ser Cys Ala His Trp His Gly Gln Gly Asp Phe  
 180 185 190  
 Tyr Val Pro Glu Met Lys Glu Thr Glu Trp Lys Trp Arg Gly Leu Val  
 195 200 205  
 25 Glu Ala Ile Asp Thr Gln Val Asp Gly Thr Gly Ala Asp Thr Met Ser  
 210 215 220  
 Asp Thr Ser Ser Val Ser Leu Glu Val Ser Pro Gly Ser Arg Glu Thr  
 225 230 235 240  
 30 Ser Ala Ala Thr Leu Ser Pro Gly Ala Ser Ser Arg Gly Trp Asp Asp  
 245 250 255  
 Gly Asp Thr Arg Ser Glu His Ser Xaa  
 260 265  
 35

40 (2) INFORMATION FOR SEQ ID NO: 176:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 138 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 176:

Met Ala Gln Leu Phe Leu Pro Leu Leu Ala Ala Leu Val Leu Ala Gln  
 1 5 10 15  
 50 Ala Pro Ala Ala Leu Ala Asp Val Leu Glu Gly Asp Ser Ser Glu Asp  
 20 25 30  
 Arg Ala Phe Arg Val Arg Ile Ala Gly Asp Ala Pro Leu Gln Gly Val  
 35 40 45  
 55 Leu Gly Gly Ala Leu Thr Ile Pro Cys His Val His Tyr Leu Arg Pro  
 50 55 60  
 60 Pro Pro Ser Arg Arg Ala Val Leu Gly Ser Pro Arg Val Lys Trp Thr  
 65 70 75 80

305

Phe Leu Ser Arg Gly Arg Glu Ala Glu Val Leu Val Ala Arg Gly Val  
                                     85                                    90                                    95

5 Arg Val Lys Val Asn Glu Ala Tyr Arg Phe Arg Val Ala Leu Pro Ala  
                                     100                                    105                                    110

Tyr Pro Ala Ser Leu Thr Asp Val Ser Pro Gly Ala Glu Arg Ala Ala  
                                     115                                    120                                    125

10 Pro Gln Arg Leu Arg Tyr Leu Ser Leu Xaa  
                                     130                                    135

15

(2) INFORMATION FOR SEQ ID NO: 177:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 179 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:

25 Met Pro Ala Leu Arg Pro Ala Leu Leu Trp Ala Leu Leu Ala Leu Trp  
       1                                    5                                    10                                    15

Leu Cys Cys Ala Thr Pro Ala His Ala Leu Gln Cys Arg Asp Gly Tyr  
                                     20                                    25                                    30

30 Glu Pro Cys Val Asn Glu Gly Met Cys Val Thr Tyr His Asn Gly Thr  
                                     35                                    40                                    45

Gly Tyr Cys Lys Gly Pro Glu Gly Phe Leu Gly Glu Tyr Cys Gln His  
                                     50                                    55                                    60

35 Arg Asp Pro Cys Glu Lys Asn Arg Cys Gln Asn Gly Gly Thr Cys Val  
       65                                    70                                    75                                    80

40 Ala Gln Ala Met Leu Gly Lys Ala Thr Cys Arg Cys Ala Ser Gly Phe  
                                     85                                    90                                    95

Thr Gly Glu Asp Cys Gln Tyr Ser Thr Ser His Pro Cys Phe Val Ser  
                                     100                                    105                                    110

45 Arg Pro Cys Leu Asn Gly Gly Thr Cys His Met Leu Ser Arg Asp Thr  
                                     115                                    120                                    125

Tyr Glu Cys Thr Cys Gln Val Gly Phe Thr Gly Lys Glu Cys Gln Trp  
                                     130                                    135                                    140

50 Thr Asp Ala Cys Leu Ser His Pro Cys Ala Asn Gly Ser Thr Cys Thr  
       145                                    150                                    155                                    160

55 Thr Val Ala Asn His Phe Leu Gln Met Pro His Arg Leu His Arg Ala  
                                     165                                    170                                    175

Glu Val Xaa

60

306

## (2) INFORMATION FOR SEQ ID NO: 178:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 155 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 178:

5 Met Thr Arg Gly Gly Pro Gly Gly Arg Pro Gly Leu Pro Gln Pro Pro  
 1 5 10 15  
 Pro Leu Leu Leu Leu Leu Leu Leu Pro Leu Leu Leu Val Thr Ala Glu  
 20 25 30  
 15 Pro Pro Lys Pro Ala Gly Val Tyr Tyr Ala Thr Ala Tyr Trp Met Pro  
 35 40 45  
 20 Ala Glu Lys Thr Val Gln Val Lys Asn Val Met Asp Lys Asn Gly Asp  
 50 55 60  
 Ala Tyr Gly Phe Tyr Asn Asn Ser Val Lys Thr Thr Gly Trp Gly Ile  
 65 70 75 80  
 25 Leu Glu Ile Arg Ala Gly Tyr Gly Ser Gln Thr Leu Ser Asn Glu Ile  
 85 90 95  
 Ile Met Phe Val Ala Gly Phe Leu Glu Gly Tyr Leu Ile Ala Pro His  
 100 105 110  
 30 Met Asn Asp His Tyr Thr Asn Leu Tyr Pro Gln Leu Ile Thr Lys Pro  
 115 120 125  
 Ser Ile Met Asp Lys Val Gln Asp Phe Met Glu Lys Gln Asp Lys Val  
 130 135 140  
 Asp Pro Glu Lys Tyr Gln Arg Ile Gln Asp Xaa  
 145 150 155

40

## (2) INFORMATION FOR SEQ ID NO: 179:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 295 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 179:

45 Met Leu Gln Gly Pro Gly Ser Leu Leu Leu Leu Phe Leu Ala Ser His  
 1 5 10 15  
 Cys Cys Leu Gly Ser Ala Arg Gly Leu Phe Leu Phe Gly Gln Pro Asp  
 20 25 30  
 55 Phe Ser Tyr Lys Arg Xaa Asn Cys Lys Pro Ile Pro Val Asn Leu Gln  
 35 40 45  
 60 Leu Cys His Gly Ile Glu Tyr Gln Asn Met Arg Leu Pro Asn Leu Leu  
 50 55 60



307

Gly His Glu Thr Met Lys Glu Val Leu Glu Gln Ala Gly Ala Trp Ile  
 65 70 75 80  
 5 Pro Leu Val Met Lys Gln Cys His Pro Asp Thr Lys Lys Phe Leu Cys  
 85 90 95  
 Ser Leu Phe Ala Pro Val Cys Leu Asp Asp Leu Asp Glu Thr Ile Gln  
 100 105 110  
 10 Pro Cys His Ser Leu Cys Val Gln Val Lys Asp Arg Cys Ala Pro Val  
 115 120 125  
 Met Ser Ala Phe Gly Phe Pro Trp Pro Asp Met Leu Glu Cys Asp Arg  
 130 135 140  
 15 Phe Pro Gln Asp Asn Asp Leu Cys Ile Pro Leu Ala Ser Ser Asp His  
 145 150 155 160  
 20 Leu Leu Pro Ala Thr Glu Glu Ala Pro Lys Val Cys Glu Ala Cys Lys  
 165 170 175  
 Asn Lys Asn Asp Asp Asp Asn Asp Ile Met Glu Thr Leu Cys Lys Asn  
 180 185 190  
 25 Asp Phe Ala Leu Lys Ile Lys Val Lys Glu Ile Thr Tyr Ile Asn Arg  
 195 200 205  
 Asp Thr Lys Ile Ile Leu Glu Thr Lys Ser Lys Thr Ile Tyr Lys Leu  
 210 215 220  
 30 Asn Gly Val Ser Glu Arg Asp Leu Lys Lys Ser Val Leu Trp Leu Lys  
 225 230 235 240  
 35 Asp Ser Leu Gln Cys Thr Cys Glu Glu Met Asn Asp Ile Asn Ala Pro  
 245 250 255  
 Tyr Leu Val Met Gly Gln Lys Gln Gly Gly Glu Leu Val Ile Thr Ser  
 260 265 270  
 40 Val Lys Arg Trp Gln Lys Gly Gln Arg Glu Phe Lys Arg Ile Ser Arg  
 275 280 285  
 Ser Ile Arg Lys Leu Gln Cys  
 290 295  
 45

(2) INFORMATION FOR SEQ ID NO: 180:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 256 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 180:

Met Arg Pro Ala Ala Leu Arg Gly Ala Leu Leu Gly Cys Leu Cys Leu  
 1 5 10 15

60 Ala Leu Leu Cys Leu Gly Gly Ala Asp Lys Arg Leu Arg Asp Asn His

308

[illegible]

50 (2) INFORMATION FOR SEQ ID NO: 181:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 324 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 181:

Met Ala Pro Leu Leu Leu Gln Leu Ala Val Leu Gly Ala Ala Leu Ala  
1 5 10 15

60

309

Ala Ala Ala Leu Val Leu Ile Ser Ile Val Ala Phe Thr Thr Ala Thr  
20 25 30

5 Lys Met Pro Ala Leu His Arg His Glu Glu Glu Lys Phe Phe Leu Asn  
35 40 45

Ala Lys Gly Gln Lys Glu Thr Leu Pro Ser Ile Trp Asp Ser Pro Thr  
50 55 60

10 Lys Gln Leu Ser Val Val Val Pro Ser Tyr Asn Glu Glu Lys Arg Leu  
65 70 75 80

Pro Val Met Met Asp Glu Ala Leu Ser Tyr Leu Glu Lys Arg Gln Lys  
85 90 95

15 Arg Asp Pro Ala Phe Thr Tyr Glu Val Ile Val Val Asp Asp Gly Ser  
100 105 110

20 Lys Asp Gln Thr Ser Lys Val Ala Phe Lys Tyr Cys Gln Lys Tyr Gly  
115 120 125

Ser Asp Lys Val Arg Val Ile Thr Leu Val Lys Asn Arg Gly Lys Gly  
130 135 140

25 Gly Ala Ile Arg Met Gly Ile Phe Ser Ser Arg Gly Glu Lys Ile Leu  
145 150 155 160

Met Ala Asp Ala Asp Gly Ala Thr Lys Phe Pro Asp Val Glu Lys Leu  
165 170 175

30 Glu Lys Gly Leu Asn Asp Leu Gln Pro Trp Pro Asn Gln Met Ala Ile  
180 185 190

Ala Cys Gly Ser Arg Ala His Leu Glu Lys Glu Ser Ile Ala Gln Arg  
195 200 205

35 Ser Tyr Phe Arg Thr Leu Leu Met Tyr Gly Phe His Phe Leu Val Trp  
210 215 220

40 Phe Leu Cys Val Lys Gly Ile Arg Asp Thr Gln Cys Gly Phe Lys Leu  
225 230 235 240

Phe Thr Arg Glu Ala Ala Ser Arg Thr Phe Ser Ser Leu His Val Glu  
245 250 255

45 Arg Trp Ala Phe Asp Val Glu Leu Leu Tyr Ile Ala Gln Phe Phe Lys  
260 265 270

Ile Pro Ile Ala Glu Ile Ala Val Asn Trp Thr Glu Ile Glu Gly Ser  
275 280 285

50 Lys Leu Val Pro Phe Trp Ser Trp Leu Gln Met Gly Lys Asp Leu Leu  
290 295 300

55 Phe Ile Arg Leu Arg Tyr Leu Thr Gly Ala Trp Arg Leu Glu Gln Thr  
305 310 315 320

Arg Lys Met Asn

60

(2) INFORMATION FOR SEQ ID NO: 182:

- 5 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 47 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 182:

10 Met Asp Ile Cys Phe Phe His Tyr Val Leu Leu Phe Phe Leu Val Arg  
 1 5 10 15  
 15 Cys Ala Leu Val Val Leu Ile Leu Leu Cys Gln Gly Trp Gly Asn Gly  
 20 25 30  
 Gly Gly Cys Val Gly Arg Val Leu Ile Ile Val Phe Ser Ser Val  
 35 40 45

20

(2) INFORMATION FOR SEQ ID NO: 183:

- 25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 93 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 183:

30 Met Ala Ser Leu Gly His Ile Leu Val Phe Cys Val Gly Leu Leu Thr  
 1 5 10 15  
 Met Ala Lys Ala Glu Ser Pro Lys Glu His Asp Pro Phe Thr Tyr Asp  
 20 25 30  
 35 Tyr Gln Ser Leu Gln Ile Gly Gly Leu Val Ile Ala Gly Ile Leu Phe  
 35 40 45  
 Ile Leu Gly Ile Leu Ile Val Leu Ser Arg Arg Cys Arg Cys Lys Phe  
 40 50 55 60  
 Asn Gln Gln Gln Arg Thr Gly Glu Pro Asp Glu Glu Glu Gly Thr Phe  
 65 70 75 80  
 45 Arg Ser Ser Ile Arg Arg Leu Ser Thr Arg Arg Arg Xaa  
 85 90

50 (2) INFORMATION FOR SEQ ID NO: 184:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 168 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

55 Met Xaa Thr Lys Glu Phe Gly Xaa Gly Arg Ala Val Gln Gln Val Leu  
 1 5 10 15  
 60

311

Asn Ile Glu Cys Leu Arg Asp Phe Leu Thr Pro Pro Leu Leu Ser Val  
 20 25 30  
 5 Arg Phe Arg Tyr Val Gly Ala Pro Gln Ala Leu Thr Leu Lys Leu Pro  
 35 40 45  
 Val Thr Xaa Asn Lys Phe Phe Gln Pro Thr Glu Met Ala Ala Gln Asp  
 50 55 60  
 10 Phe Phe Gln Arg Trp Lys Gln Leu Ser Leu Pro Gln Gln Glu Ala Gln  
 65 70 75 80  
 Lys Ile Phe Lys Ala Asn His Pro Met Asp Ala Glu Val Thr Lys Ala  
 85 90 95  
 15 Lys Leu Leu Gly Phe Gly Ser Ala Leu Leu Asp Asn Val Asp Pro Asn  
 100 105 110  
 Pro Glu Asn Phe Val Gly Ala Gly Ile Ile Gln Thr Lys Ala Leu Gln  
 115 120 125  
 Val Gly Cys Leu Leu Arg Leu Glu Pro Asn Ala Gln Ala Gln Met Tyr  
 130 135 140  
 25 Arg Leu Thr Leu Arg Thr Ser Lys Glu Pro Val Ser Arg His Leu Cys  
 145 150 155 160  
 Glu Leu Leu Ala Gln Gln Phe Xaa  
 165

30

(2) INFORMATION FOR SEQ ID NO: 185:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 43 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 185:

40

Met Phe Tyr Val Leu Ser Val Ser Pro Leu Leu Xaa Phe Leu Ala Cys  
 1 5 10 15

45

Gly Leu Cys Leu Cys Val Asn Trp Lys Ile Ala Ile Ser Gln Leu Ser  
 20 25 30

Leu Ser Phe Lys Asn Glu Leu Glu Lys Pro Xaa  
 35 40

50

(2) INFORMATION FOR SEQ ID NO: 186:

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 59 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186:

60

Met Lys Leu Phe Asp Ala Ser Pro Thr Phe Phe Ala Phe Leu Leu Gly

312

1                      5                      10                      15  
 His Ile Leu Ala Met Glu Val Leu Ala Trp Leu Leu Ile Tyr Leu Leu  
                          20                                      25                                      30  
 5 Gly Pro Gly Trp Val Pro Ser Ala Leu Xaa Arg Leu His Pro Gly His  
                          35                                      40                                      45  
 10 Leu Ser Gly Ser Val Leu Val Ser Ala Ala Xaa  
                          50                                      55

(2) INFORMATION FOR SEQ ID NO: 187:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 189 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 187:

Met Asp Val Asn Ile Ala Pro Leu Arg Ala Trp Asp Asp Phe Phe Pro  
                          1                                      5                                      10                                      15  
 25 Gly Ser Asp Arg Phe Ala Arg Pro Asp Phe Arg Asp Ile Ser Lys Trp  
                          20                                      25                                      30  
 Asn Asn Arg Val Val Ser Asn Leu Leu Tyr Tyr Gln Thr Asn Tyr Leu  
                          35                                      40                                      45  
 30 Val Val Ala Ala Met Met Ile Ser Ile Val Gly Phe Leu Ser Pro Phe  
                          50                                      55                                      60  
 Asn Met Ile Leu Gly Gly Ile Val Val Val Leu Val Phe Thr Gly Phe  
                          65                                      70                                      75                                      80  
 Val Trp Ala Ala His Asn Lys Asp Val Leu Arg Arg Met Lys Lys Arg  
                          85                                      90                                      95  
 40 Tyr Pro Thr Thr Phe Val Met Val Val Met Leu Ala Ser Tyr Phe Leu  
                          100                                      105                                      110  
 Ile Ser Met Phe Gly Gly Val Met Val Phe Val Phe Gly Ile Thr Phe  
                          115                                      120                                      125  
 45 Pro Leu Leu Leu Met Phe Ile His Ala Ser Leu Arg Leu Arg Asn Leu  
                          130                                      135                                      140  
 Lys Asn Lys Leu Glu Asn Lys Met Glu Gly Ile Gly Leu Lys Arg Thr  
                          145                                      150                                      155                                      160  
 Pro Met Gly Ile Val Leu Asp Ala Leu Glu Gln Gln Glu Glu Gly Ile  
                          165                                      170                                      175  
 55 Asn Arg Leu Thr Asp Tyr Ile Ser Lys Val Lys Glu Xaa  
                          180                                      185

60 (2) INFORMATION FOR SEQ ID NO: 188:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 146 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188:

Met Phe Leu Thr Arg Ile Leu Cys Pro Thr Tyr Ile Ala Leu Thr Phe  
 1 5 10 15  
 Leu Val Tyr Ile Val Ala Leu Val Ser Gly Gln Leu Cys Met Glu Ile  
 20 25 30  
 Ala Arg Gly Asn Ile Phe Phe Leu Asn Glu Leu Val Thr Thr Phe Cys  
 35 40 45  
 Cys Ser Cys Leu Leu Leu Ser Val Pro Tyr Leu His Pro Gly Phe Phe  
 50 55 60  
 Tyr Ser Ser Leu Cys Lys Cys Cys Phe Val Leu Val Val Leu Ser Arg  
 65 70 75 80  
 Ile Gly Ser Val Asn Glu Thr Trp Ser Cys Asn Phe Ser Ile Cys Ser  
 85 90 95  
 Tyr Leu Ile Phe Gly Ser Pro Ile Phe Thr Ala Val Ile Pro Lys Arg  
 100 105 110  
 Cys Ala Leu Glu Asp Ile Gln Asn Asn Pro Ile Gly Cys Leu Leu Arg  
 115 120 125  
 Cys Thr Pro Ala Trp Glu Thr Glu Gly Asp Ser Ile Ser Lys Lys Ile  
 130 135 140  
 Lys Lys  
 145

## (2) INFORMATION FOR SEQ ID NO: 189:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 84 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 189:

Met Gly Ser Arg Ala Glu Leu Cys Thr Leu Leu Gly Gly Phe Ser Phe  
 1 5 10 15  
 Leu Leu Leu Leu Ile Pro Gly Glu Gly Ala Lys Gly Gly Ser Leu Arg  
 20 25 30  
 Glu Ser Gln Gly Val Cys Ser Lys Gln Thr Leu Val Val Pro Leu His  
 35 40 45  
 Tyr Asn Glu Ser Tyr Ser Gln Pro Val Tyr Lys Pro Tyr Leu Thr Leu  
 50 55 60  
 Cys Ala Gly Ser Ala Ser Ala Ala Leu Thr Gly Pro Cys Thr Ala Leu  
 60

314

65

70

75

80

Cys Gly Gly Arg

5

(2) INFORMATION FOR SEQ ID NO: 190:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 58 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:

15

Met Met Gly Val Leu Gln Leu Leu His Ile Phe Trp Ala Tyr Leu Ile  
 1 5 10 15

20

Leu Arg Met Ala His Lys Phe Ile Thr Gly Lys Leu Val Glu Asp Glu  
 20 25 30

Arg Ser Thr Gly Lys Lys Gln Arg Ala Gln Arg Gly Arg Arg Leu Gln  
 35 40 45

25

Leu Gly Glu Glu Gln Arg Ala Gly Pro Xaa  
 50 55

30

(2) INFORMATION FOR SEQ ID NO: 191:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 311 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 191:

40

Met Arg Arg Leu Val His Asp Leu Leu Pro Pro Glu Val Cys Ser Leu  
 1 5 10 15

Leu Asn Pro Ala Ala Ile Tyr Ala Asn Asn Glu Ile Ser Leu Arg Asp  
 20 25 30

45

Val Glu Val Tyr Gly Phe Asp Tyr Asp Tyr Thr Leu Ala Gln Tyr Ala  
 35 40 45

Asp Ala Leu His Pro Glu Ile Phe Ser Thr Ala Arg Asp Ile Leu Ile  
 50 55 60

50

Glu His Tyr Lys Tyr Pro Glu Gly Ile Arg Lys Tyr Asp Tyr Asn Pro  
 65 70 75 80

Ser Phe Ala Ile Arg Gly Leu His Tyr Asp Ile Gln Lys Ser Leu Leu  
 85 90 95

55

Met Lys Ile Asp Ala Phe His Tyr Val Gln Leu Gly Thr Ala Tyr Arg  
 100 105 110

60

Gly Leu Gln Pro Val Pro Asp Glu Glu Val Ile Glu Leu Tyr Gly Gly  
 115 120 125



315

Thr Gln His Ile Pro Leu Tyr Gln Met Ser Gly Phe Tyr Gly Lys Gly  
 130 135 140  
 5 Pro Ser Ile Lys Gln Phe Met Asp Ile Phe Ser Leu Pro Glu Met Ala  
 145 150 155 160  
 Leu Leu Ser Cys Val Val Asp Tyr Phe Leu Gly His Ser Leu Glu Phe  
 165 170 175  
 10 Asp Gln Ala His Leu Tyr Lys Asp Val Thr Asp Ala Ile Arg Asp Val  
 180 185 190  
 His Val Lys Gly Leu Met Tyr Gln Trp Ile Glu Gln Asp Met Glu Lys  
 195 200 205  
 15 Tyr Ile Leu Arg Gly Asp Glu Thr Phe Ala Val Leu Ser Arg Leu Val  
 210 215 220  
 20 Ala His Gly Lys Gln Leu Phe Leu Ile Thr Asn Ser Pro Phe Ser Phe  
 225 230 235 240  
 Val Asp Lys Gly Met Arg His Met Val Gly Pro Asp Trp Arg His Ser  
 245 250 255  
 25 Ser Met Trp Ser Leu Ser Arg Gln Thr Ser Pro Ala Ser Ser Leu Thr  
 260 265 270  
 Gly Ala Ser Phe Xaa Glu Asn Ser Met Arg Arg Ala His Phe Ser Gly  
 275 280 285  
 30 Thr Gly Ser Pro Ala Trp Lys Arg Ala Arg Ser Ile Gly Arg Glu Thr  
 290 295 300  
 35 Cys Leu Thr Ser Tyr Ala Xaa  
 305 310

40 (2) INFORMATION FOR SEQ ID NO: 192:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 318 amino acids

(B) TYPE: amino acid

45 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu  
 1 5 10 15  
 50 Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu  
 20 25 30  
 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu  
 35 40 45  
 55 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu  
 50 55 60  
 60 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser

316

	65					70						75					80
	Ala	Arg	Arg	Val	His	Glu	Leu	Glu	Arg	Val	Lys	Arg	Arg	Cys	Leu	Glu	
					85					90					95		
5	Asn	Gly	Asn	Leu	Lys	Glu	Lys	Asp	Ile	Leu	Val	Leu	Pro	Leu	Asp	Leu	
				100				105						110			
10	Thr	Asp	Thr	Gly	Ser	His	Glu	Ala	Ala	Thr	Lys	Ala	Val	Leu	Gln	Glu	
			115					120					125				
	Phe	Gly	Arg	Ile	Asp	Ile	Leu	Val	Asn	Asn	Gly	Gly	Met	Ser	Gln	Arg	
		130					135					140					
15	Ser	Leu	Cys	Met	Asp	Thr	Ser	Leu	Asp	Val	Tyr	Arg	Lys	Leu	Ile	Glu	
	145					150					155					160	
	Leu	Asn	Tyr	Leu	Gly	Thr	Val	Ser	Leu	Thr	Lys	Cys	Val	Leu	Pro	His	
					165					170					175		
20	Met	Ile	Glu	Arg	Lys	Gln	Gly	Lys	Ile	Val	Thr	Val	Asn	Ser	Ile	Leu	
				180				185						190			
	Gly	Ile	Ile	Ser	Val	Pro	Leu	Ser	Ile	Gly	Tyr	Cys	Ala	Ser	Lys	His	
25			195					200					205				
	Ala	Leu	Arg	Gly	Phe	Phe	Asn	Gly	Leu	Arg	Thr	Glu	Leu	Ala	Thr	Tyr	
		210					215					220					
30	Pro	Gly	Ile	Ile	Val	Ser	Asn	Ile	Cys	Pro	Gly	Pro	Val	Gln	Ser	Asn	
	225					230					235					240	
	Ile	Val	Glu	Asn	Ser	Leu	Ala	Gly	Glu	Val	Thr	Lys	Thr	Ile	Gly	Asn	
					245					250					255		
35	Asn	Gly	Asp	Gln	Ser	His	Lys	Met	Thr	Thr	Ser	Arg	Cys	Val	Arg	Leu	
				260					265					270			
40	Met	Leu	Ile	Ser	Met	Ala	Asn	Asp	Leu	Lys	Glu	Val	Trp	Ile	Ser	Glu	
		275						280					285				
	Gln	Pro	Phe	Leu	Phe	Ser	Asn	Ile	Phe	Val	Ala	Ile	His	Ala	Asn	Leu	
		290					295					300					
45	Gly	Leu	Val	Asp	Asn	Gln	Gln	Asp	Gly	Glu	Glu	Lys	Asp	Xaa			
	305					310					315						

50 (2) INFORMATION FOR SEQ ID NO: 193:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 53 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 193:

Met Trp Pro Ser Phe Pro Gln Val Arg Val Gly Ser Phe Leu Phe Gly  
1 5 10 15

60

317

Ile Leu Phe Phe Ser Phe Gly Ser Ser Ser Leu Pro Pro Gly Leu Pro  
20 25 30

5 Pro Pro Ala Ser Leu Leu Cys Cys Ala Val Gln Trp Gly Ala Arg Ala  
35 40 45

Leu Phe Leu Pro Ala  
50

10

(2) INFORMATION FOR SEQ ID NO: 194:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 42 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:

20 Met Leu Val Thr Cys Ser Val Cys Cys Tyr Leu Phe Trp Leu Ile Ala  
1 5 10 15

Ile Leu Ala Gln Leu Asn Pro Leu Phe Gly Pro Gln Leu Lys Asn Glu  
20 25 30

25

Thr Ile Trp Tyr Leu Lys Tyr His Trp Pro  
35 40

30

(2) INFORMATION FOR SEQ ID NO: 195:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 102 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 195:

40 Met Glu Gly Thr Glu Met Gly Ala Arg Pro Gly Gly His Pro Gln Lys  
1 5 10 15

Trp Ser Phe Leu Trp Ser Leu Ala Leu Trp Leu Pro Leu Ala Leu Ser  
20 25 30

45 Val Ser Leu Phe Leu Gly Leu Ser Leu Ser Pro Pro Gln Pro Gly Leu  
35 40 45

Ser Leu Trp Cys Thr Leu Ser Tyr Cys Cys Glu Gln Trp Lys Phe Lys  
50 55 60

50

Gly Thr Pro Ser Pro Ala Leu Leu Asn Leu Gly Thr Gln Pro Lys Lys  
65 70 75 80

55 Asp Lys Lys Leu Glu Asp Ser Ile Ala Thr Gln Leu Arg Glu Leu Pro  
85 90 95

Glu Lys Asn Ser Asn Xaa  
100

60

## (2) INFORMATION FOR SEQ ID NO: 196:

## (i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 45 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196:

10 Met Ala Leu Thr Phe Leu Leu Val Leu Leu Thr Leu Ala Thr Ser Ala  
1 5 10 15  
His Gly Cys Thr Glu Thr Ser Asp Ala Gly Arg Ala Ser Thr Gly Gly  
20 25 30  
15 Pro Gln Arg Thr Ala Arg Thr Gln Trp Leu Leu Cys Xaa  
35 40 45

20

## (2) INFORMATION FOR SEQ ID NO: 197:

## (i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 355 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:

30 Met Gly Pro Ser Thr Pro Leu Leu Ile Leu Phe Leu Leu Ser Trp Ser  
1 5 10 15  
Gly Pro Leu Gln Gly Gln Gln His His Leu Val Glu Tyr Met Glu Arg  
20 25 30  
35 Arg Leu Ala Ala Leu Glu Glu Arg Leu Ala Gln Cys Gln Asp Gln Ser  
35 40 45  
Ser Arg His Ala Ala Glu Leu Arg Asp Phe Lys Asn Lys Met Leu Pro  
50 55 60  
40 Leu Leu Glu Val Ala Glu Lys Glu Arg Glu Ala Leu Arg Thr Glu Ala  
65 70 75 80  
Asp Thr Ile Ser Gly Arg Val Asp Arg Leu Glu Arg Glu Val Asp Tyr  
45 85 90 95  
Leu Glu Thr Gln Asn Pro Ala Leu Pro Cys Val Glu Phe Asp Glu Lys  
100 105 110  
50 Val Thr Gly Gly Pro Gly Thr Lys Gly Lys Gly Arg Arg Asn Glu Lys  
115 120 125  
Tyr Asp Met Val Thr Asp Cys Gly Tyr Thr Ile Ser Gln Val Arg Ser  
130 135 140  
55 Met Lys Ile Leu Lys Arg Phe Gly Gly Pro Ala Gly Leu Trp Thr Lys  
145 150 155 160  
Asp Pro Leu Gly Gln Thr Glu Lys Ile Tyr Val Leu Asp Gly Thr Gln  
60 165 170 175

319

Asn Asp Thr Ala Phe Val Phe Pro Arg Leu Arg Asp Phe Thr Leu Ala  
 180 185 190

5 Met Ala Ala Arg Lys Ala Ser Arg Val Arg Val Pro Phe Pro Trp Val  
 195 200 205

Gly Thr Gly Gln Leu Val Tyr Gly Gly Phe Leu Tyr Phe Ala Arg Arg  
 210 215 220

10 Pro Pro Gly Arg Pro Gly Gly Gly Gly Glu Met Glu Asn Thr Leu Gln  
 225 230 235 240

Leu Ile Lys Phe His Leu Ala Asn Arg Thr Val Val Asp Ser Ser Val  
 15 245 250 255

Phe Pro Ala Glu Gly Leu Ile Pro Pro Tyr Gly Leu Thr Ala Asp Thr  
 260 265 270

20 Tyr Ile Asp Leu Ala Ala Asp Glu Gly Leu Trp Ala Val Tyr Ala  
 275 280 285

Thr Arg Glu Asp Asp Arg His Leu Cys Leu Ala Lys Leu Asp Pro Gln  
 290 295 300

25 Thr Leu Asp Thr Glu Gln Gln Trp Asp Thr Pro Cys Pro Arg Glu Asn  
 305 310 315 320

Ala Glu Ala Ala Phe Val Ile Cys Gly Thr Leu Tyr Val Val Tyr Asn  
 30 325 330 335

Thr Arg Pro Ala Ser Arg Ala Arg Ile Gln Cys Ser Phe Asp Ala Ser  
 340 345 350

35 Gly Pro Xaa  
 355

40 (2) INFORMATION FOR SEQ ID NO: 198:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 74 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:

Met Val Leu Pro Leu Leu Ile Phe Val Leu Leu Pro Lys Val Val Asn  
 1 5 10 15

50 Thr Ser Asp Pro Asp Met Arg Arg Glu Met Glu Gln Ser Met Asn Met  
 20 25 30

Leu Asn Ser Asn His Glu Leu Pro Asp Val Ser Glu Phe Met Thr Arg  
 35 40 45

55 Leu Phe Ser Ser Lys Ser Ser Gly Lys Ser Ser Ser Gly Ser Ser Lys  
 50 55 60

60 Thr Gly Lys Ser Gly Ala Gly Lys Arg Arg

65

70

## 5 (2) INFORMATION FOR SEQ ID NO: 199:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 113 amino acids

(B) TYPE: amino acid

10 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

Met Phe Thr Met Leu Cys Ile Asn Gly Thr Thr Pro Arg Pro Leu Pro  
 1 5 10 15  
 Val Pro Ser Pro Phe Gly Cys Met Ile Phe Phe Phe Phe Lys Asn Pro  
 20 25 30  
 Trp Lys Gln Arg Leu Leu Gln Gly Trp Leu Gly Ala Arg Pro Ile His  
 35 40 45  
 Leu Leu Gly Tyr Leu Pro Leu Ser Leu Leu Trp Cys Pro Phe Pro Leu  
 50 55 60  
 Pro Cys Ala Arg Cys Ser Val Val Tyr Ile Ser Ser Pro Arg His Gly  
 65 70 75 80  
 Ala His Ala Pro Arg Asp Met Ile Leu Ser Leu Val Leu Ala His Gly  
 85 90 95  
 Ala Leu Tyr Lys Glu Leu Gly Gly Arg Gly Arg Lys Trp Glu Pro Ser  
 100 105 110

Xaa

35

## 40 (2) INFORMATION FOR SEQ ID NO: 200:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 123 amino acids

(B) TYPE: amino acid

45 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 200:

Met Ala Cys Arg Cys Leu Ser Phe Leu Leu Met Gly Thr Phe Leu Ser  
 1 5 10 15  
 Val Ser Gln Thr Val Leu Ala Gln Leu Asp Ala Leu Leu Val Phe Pro  
 20 25 30  
 Gly Gln Val Ala Gln Leu Ser Cys Thr Leu Ser Pro Gln His Val Thr  
 35 40 45  
 Ile Arg Asp Tyr Gly Val Ser Trp Tyr Gln Gln Arg Ala Gly Ser Ala  
 50 55 60  
 Pro Arg Tyr Leu Leu Tyr Tyr Arg Ser Glu Glu Asp His His Arg Pro  
 65 70 75 80

321

Ala Asp Ile Pro Asp Arg Phe Ser Ala Ala Lys Asp Glu Ala His Asn  
                                     85                                    90                                    95

5 Ala Cys Val Leu Thr Ile Ser Pro Val Gln Pro Glu Asp Asp Ala Asp  
                                     100                                    105                                    110

Tyr Tyr Cys Ser Val Gly Tyr Gly Phe Ser Pro  
                                     115                                    120

10

(2) INFORMATION FOR SEQ ID NO: 201:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 315 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 201:

20

Met Ala Gly Gly Arg Cys Gly Pro Xaa Leu Thr Ala Leu Leu Ala Ala  
   1                                    5                                    10                                    15

25

Trp Ile Ala Ala Val Ala Ala Thr Ala Gly Pro Glu Glu Ala Ala Leu  
                                     20                                    25                                    30

Pro Pro Glu Gln Ser Arg Val Gln Pro Met Thr Ala Ser Asn Trp Thr  
                                     35                                    40                                    45

30

Leu Val Met Glu Gly Glu Trp Met Leu Lys Phe Tyr Ala Pro Trp Cys  
                                     50                                    55                                    60

Pro Ser Cys Gln Gln Thr Asp Ser Glu Trp Glu Ala Phe Ala Lys Asn  
                                     65                                    70                                    75                                    80

35

Gly Glu Ile Leu Gln Ile Ser Val Gly Lys Val Asp Val Ile Gln Glu  
                                     85                                    90                                    95

40

Pro Gly Leu Ser Gly Arg Phe Phe Val Thr Thr Leu Pro Ala Phe Phe  
                                     100                                    105                                    110

His Ala Lys Asp Gly Ile Phe Arg Arg Tyr Arg Gly Pro Gly Ile Phe  
                                     115                                    120                                    125

45

Glu Asp Leu Gln Asn Tyr Ile Leu Glu Lys Lys Trp Gln Ser Val Glu  
                                     130                                    135                                    140

Pro Leu Thr Gly Trp Lys Ser Pro Ala Ser Leu Thr Met Ser Gly Met  
                                     145                                    150                                    155                                    160

50

Ala Gly Leu Phe Ser Ile Ser Gly Lys Ile Trp His Leu His Asn Tyr  
                                     165                                    170                                    175

55

Phe Thr Val Thr Leu Gly Ile Pro Ala Trp Cys Ser Tyr Val Phe Phe  
                                     180                                    185                                    190

Val Ile Ala Thr Leu Val Phe Gly Leu Phe Met Gly Leu Val Leu Val  
                                     195                                    200                                    205

60

Val Ile Ser Glu Cys Phe Tyr Val Pro Leu Pro Arg His Leu Ser Glu

322

210                      215                      220  
 Arg Ser Glu Gln Asn Arg Arg Ser Glu Glu Ala His Arg Ala Glu Gln  
 225                      230                      235                      240  
 5    Leu Gln Asp Ala Glu Glu Glu Lys Asp Asp Ser Asn Glu Glu Glu Asn  
                                  245                      250                      255  
 10    Lys Asp Ser Leu Val Asp Asp Glu Glu Glu Lys Glu Asp Leu Gly Asp  
                                  260                      265                      270  
                                  Glu Asp Glu Ala Glu Glu Glu Glu Glu Glu Asp Asn Leu Ala Ala Gly  
                                  275                      280                      285  
 15    Val Asp Glu Glu Arg Ser Glu Ala Asn Asp Gln Gly Pro Pro Gly Glu  
                                  290                      295                      300  
                                  Asp Gly Val Thr Arg Glu Xaa Ser Arg Ala Xaa  
 20    305                      310                      315

(2) INFORMATION FOR SEQ ID NO: 202:

25                      (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 236 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:

30    Met Gly Thr Ala Asp Ser Asp Glu Met Ala Pro Glu Ala Pro Gln His  
                                  1                      5                      10                      15  
 35    Thr His Ile Asp Val His Ile His Gln Glu Ser Ala Leu Ala Lys Leu  
                                  20                      25                      30  
                                  Leu Leu Thr Cys Cys Ser Ala Leu Arg Pro Arg Ala Thr Gln Ala Arg  
                                  35                      40                      45  
 40    Gly Ser Ser Arg Leu Leu Val Ala Ser Trp Val Met Gln Ile Val Leu  
                                  50                      55                      60  
                                  Gly Ile Leu Ser Ala Val Leu Gly Gly Phe Phe Tyr Ile Arg Asp Tyr  
 45    65                      70                      75                      80  
                                  Thr Leu Leu Val Thr Ser Gly Ala Ala Ile Trp Thr Gly Ala Val Ala  
                                  85                      90                      95  
                                  Val Leu Ala Gly Ala Ala Ala Phe Ile Tyr Glu Lys Arg Gly Gly Thr  
 50    100                      105                      110  
                                  Tyr Trp Ala Leu Leu Arg Thr Leu Leu Ala Leu Ala Ala Phe Ser Thr  
                                  115                      120                      125  
 55    Ala Ile Ala Ala Leu Lys Leu Trp Asn Glu Asp Phe Arg Tyr Gly Tyr  
                                  130                      135                      140  
                                  Ser Tyr Tyr Asn Ser Ala Cys Arg Ile Ser Ser Ser Ser Asp Trp Asn  
 60    145                      150                      155                      160



323

Thr Pro Ala Pro Thr Gln Ser Pro Glu Glu Val Arg Arg Leu His Leu  
165 170 175

5 Cys Thr Ser Phe Met Asp Met Leu Lys Ala Leu Phe Arg Thr Leu Gln  
180 185 190

Ala Met Leu Leu Gly Val Trp Ile Leu Leu Leu Leu Ala Ser Leu Ala  
195 200 205

10 Pro Leu Trp Leu Tyr Cys Trp Arg Met Phe Pro Thr Lys Gly Lys Arg  
210 215 220

Asp Gln Lys Glu Met Leu Glu Val Ser Gly Ile Xaa  
225 230 235

15

(2) INFORMATION FOR SEQ ID NO: 203:

20 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 93 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 203:

25 Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala  
1 5 10 15

30 Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr  
20 25 30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro  
35 40 45

35 Leu Leu Ala Gly Leu Val Ala Ala Asp Ala Val Ala Ser Leu Leu Ile  
50 55 60

Val Gly Ala Val Phe Leu Cys Ala Arg Pro Arg Arg Ser Pro Ala Gln  
65 70 75 80

40 Glu Asp Gly Lys Val Tyr Ile Asn Met Pro Gly Arg Gly  
85 90

45

(2) INFORMATION FOR SEQ ID NO: 204:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 35 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

50 Met Trp Ser Ala Gly Arg Gly Gly Ala Ala Trp Pro Val Leu Leu Gly  
1 5 10 15

Leu Leu Leu Ala Leu Leu Val Pro Gly Gly Gly Ala Ala Lys Thr Gly  
20 25 30

60 Ala Asp Ser

35

## 5 (2) INFORMATION FOR SEQ ID NO: 205:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 43 amino acids

(B) TYPE: amino acid

10 (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

Asp Cys Xaa His Val Ser Val Leu Gln Ser Thr Ile Ser Pro Leu Leu  
 1 5 10 15  
 Pro Leu Pro Leu Leu Leu Pro His Gly Asn Cys Glu Glu Ala Pro Trp  
 20 25 30  
 Gln Ala Ala Val Ile Gly Gly Gly Asp Arg Ile  
 35 40

## 25 (2) INFORMATION FOR SEQ ID NO: 206:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 85 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

Met Arg Asp Cys Leu Ser Leu Lys Pro Arg Pro Leu Phe Pro Thr Gln  
 1 5 10 15  
 Phe Phe Phe Ile Leu Leu Leu Ile Phe Ile Ala Glu Val Ala Ala Ala  
 20 25 30  
 Val Val Ala Leu Val Tyr Thr Thr Met Val Arg His Trp Asp Gly Gly  
 35 40 45  
 Arg Glu Glu Asp Trp Ala Lys Pro Trp Glu Trp Ala Val Ala Cys Glu  
 50 55 60  
 Trp Pro Pro Ser Val Pro Ala Pro Lys His Trp Pro Ala Ser Pro Arg  
 65 70 75 80  
 Leu Ser Thr Ser Xaa  
 85

50

## (2) INFORMATION FOR SEQ ID NO: 207:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 208 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:

60 Met His Gly Asn Glu Ala Leu Gly Arg Glu Leu Leu Leu Leu Met

325

1                      5                      10                      15  
 Gln Phe Leu Cys His Glu Phe Leu Arg Xaa Asn Pro Arg Val Thr Arg  
                             20                      25                      30  
 5 Leu Leu Ser Glu Met Arg Ile His Leu Leu Pro Ser Met Asn Pro Asp  
                             35                      40                      45  
 Gly Tyr Glu Ile Ala Tyr His Arg Gly Ser Glu Leu Val Gly Trp Ala  
 10                      50                      55                      60  
 Glu Gly Arg Trp Asn Asn Gln Ser Ile Asp Leu Asn His Asn Phe Ala  
                             65                      70                      75                      80  
 15 Xaa Leu Asn Thr Pro Leu Trp Glu Ala Gln Asp Asp Gly Lys Val Pro  
                             85                      90                      95  
 His Ile Val Pro Asn His His Leu Pro Leu Pro Thr Tyr Tyr Thr Leu  
                             100                      105                      110  
 20 Pro Asn Ala Thr Val Ala Pro Glu Thr Arg Ala Val Ile Lys Trp Met  
                             115                      120                      125  
 Lys Arg Ile Pro Phe Val Leu Ser Ala Asn Leu His Gly Gly Glu Leu  
 25                      130                      135                      140  
 Val Val Ser Tyr Pro Phe Asp Met Thr Arg Thr Pro Trp Ala Ala Arg  
                             145                      150                      155                      160  
 30 Glu Leu Thr Pro Thr Pro Asp Asp Ala Val Phe Arg Trp Leu Ser Thr  
                             165                      170                      175  
 Val Tyr Ala Gly Ser Asn Leu Ala Met Gln Asp Thr Ser Arg Arg Pro  
                             180                      185                      190  
 35 Cys His Ser Gln Asp Phe Ser Val His Gly Asn Ile Ile Asn Gly Ala  
                             195                      200                      205

40

(2) INFORMATION FOR SEQ ID NO: 208:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 208:

Met Glu Ile Ser Cys Leu Leu Leu Leu Ile Gln Asp Ser Asp Glu Met  
 1                      5                      10                      15

55

Glu Asp Gly Pro Gly Val Gln Asp  
 20

60

(2) INFORMATION FOR SEQ ID NO: 209:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 483 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

5 Met Ala Thr Gly Gly Gly Ile Arg Ala Met Thr Ser Leu Tyr Gly Gln  
 1 5 10 15  
 10 Leu Ala Gly Leu Lys Glu Leu Gly Leu Leu Asp Cys Xaa Ser Tyr Ile  
 20 25 30  
 15 Thr Gly Ala Ser Gly Ser Thr Trp Ala Leu Ala Asn Leu Tyr Lys Asp  
 35 40 45  
 Pro Glu Trp Ser Gln Lys Asp Leu Ala Gly Pro Thr Glu Leu Leu Lys  
 50 55 60  
 20 Thr Gln Val Thr Lys Asn Lys Leu Gly Val Leu Ala Pro Ser Gln Leu  
 65 70 75 80  
 Gln Arg Tyr Arg Gln Glu Leu Ala Glu Arg Ala Arg Leu Gly Tyr Pro  
 85 90 95  
 25 Ser Cys Phe Thr Asn Leu Trp Ala Leu Ile Asn Glu Ala Leu Leu His  
 100 105 110  
 Asp Glu Pro His Asp His Lys Leu Ser Asp Gln Arg Glu Ala Leu Ser  
 115 120 125  
 30 His Gly Gln Asn Pro Leu Pro Ile Tyr Cys Ala Leu Asn Thr Lys Gly  
 130 135 140  
 35 Gln Ser Leu Thr Thr Phe Glu Phe Gly Glu Trp Cys Glu Phe Ser Pro  
 145 150 155 160  
 Tyr Glu Val Gly Phe Pro Lys Tyr Gly Ala Phe Ile Pro Ser Glu Leu  
 165 170 175  
 40 Phe Gly Ser Glu Phe Phe Met Gly Gln Leu Met Lys Arg Leu Pro Glu  
 180 185 190  
 45 Ser Arg Ile Cys Phe Leu Glu Gly Ile Trp Ser Asn Leu Tyr Ala Ala  
 195 200 205  
 Asn Leu Gln Asp Ser Leu Tyr Trp Ala Ser Glu Pro Ser Gln Phe Trp  
 210 215 220  
 50 Asp Arg Trp Val Arg Asn Gln Ala Asn Leu Asp Lys Glu Gln Val Pro  
 225 230 235 240  
 Leu Leu Lys Ile Glu Glu Pro Pro Ser Thr Ala Gly Arg Ile Ala Glu  
 245 250 255  
 55 Phe Phe Thr Asp Leu Leu Thr Trp Arg Pro Leu Ala Gln Ala Thr His  
 260 265 270  
 60 Asn Phe Leu Arg Gly Leu His Phe His Lys Asp Tyr Phe Gln His Pro  
 275 280 285

327

His Phe Ser Thr Trp Lys Ala Thr Thr Leu Asp Gly Leu Pro Asn Gln  
 290 295 300  
 5 Leu Thr Pro Ser Glu Pro His Leu Cys Leu Leu Asp Val Gly Tyr Leu  
 305 310 315 320  
 Ile Asn Thr Ser Cys Leu Pro Leu Leu Gln Pro Thr Arg Asp Val Asp  
 325 330 335  
 10 Leu Ile Leu Ser Leu Asp Tyr Asn Leu His Gly Ala Phe Gln Gln Leu  
 340 345 350  
 Gln Leu Leu Gly Arg Phe Cys Gln Glu Gln Gly Ile Pro Phe Pro Pro  
 355 360 365  
 15 Ile Ser Pro Ser Pro Glu Glu Gln Leu Gln Pro Arg Glu Cys His Thr  
 370 375 380  
 20 Phe Ser Asp Pro Thr Cys Pro Gly Ala Pro Ala Val Leu His Phe Pro  
 385 390 395 400  
 Leu Val Ser Asp Ser Phe Arg Glu Tyr Ser Ala Pro Gly Val Arg Arg  
 405 410 415  
 25 Thr Pro Glu Glu Ala Ala Ala Gly Glu Val Asn Leu Ser Ser Ser Asp  
 420 425 430  
 Ser Pro Tyr His Tyr Thr Lys Val Thr Tyr Ser Gln Glu Asp Val Asp  
 435 440 445  
 30 Lys Leu Leu His Leu Thr His Tyr Asn Val Cys Asn Asn Gln Glu Gln  
 450 455 460  
 35 Leu Leu Glu Ala Leu Arg Gln Ala Val Gln Arg Arg Arg Gln Arg Arg  
 465 470 475 480  
 Pro His Xaa

40

(2) INFORMATION FOR SEQ ID NO: 210:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 13 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 210:

50

Leu Glu Val Gly Cys Ile Gln Val Ala Pro Asp Thr Phe  
 1 5 10

55

(2) INFORMATION FOR SEQ ID NO: 211:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 amino acids

(B) TYPE: amino acid

60

328

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

5 Met Ser Leu Phe Phe Leu Leu Thr Leu Ile Ser Lys Leu His Gly Asp  
 1 5 10 15  
 Ala Glu Val Cys  
 20

10

(2) INFORMATION FOR SEQ ID NO: 212:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 55 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 55 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

20 Met Pro His Pro Pro Leu Pro Glu Thr Ser Leu Glu Ala Gln Leu Pro  
 1 5 10 15  
 Met Gly Leu Leu Gln Leu Leu Arg Cys Ser Val Gln Ala Trp Ser Pro  
 20 25 30  
 25 Pro Pro Ser Ser Phe Cys Pro Gly Ser Glu Pro Arg Ser Ala Ser Ala  
 35 40 45  
 30 His Trp Gly Tyr Trp Trp Pro  
 50 55

(2) INFORMATION FOR SEQ ID NO: 213:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 35 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 213:

40 Asp Pro Glu Thr Arg Trp His His Gly Gly Ser Ala Gln Asn Gly Leu  
 1 5 10 15  
 45 Leu Met Leu Ile Ser Val Leu Gln Gln Pro Val Ile Gly Thr Gly Ser  
 20 25 30  
 Tyr Leu Cys  
 35

50

(2) INFORMATION FOR SEQ ID NO: 214:

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 230 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 214:

60

329

Met Glu Pro Leu Arg Leu Leu Ile Leu Leu Phe Val Thr Glu Leu Ser  
 1 5 10 15  
 Gly Ala His Asn Thr Thr Val Phe Gln Gly Val Ala Gly Gln Ser Leu  
 5 20 25 30  
 Gln Val Ser Cys Pro Tyr Asp Ser Met Lys His Trp Gly Arg Arg Lys  
 35 40 45  
 Ala Trp Cys Arg Gln Leu Gly Glu Lys Gly Pro Cys Gln Arg Val Val  
 10 50 55 60  
 Ser Thr His Asn Leu Trp Leu Leu Ser Phe Leu Arg Arg Trp Asn Gly  
 65 70 75 80  
 15 Ser Thr Ala Ile Thr Asp Asp Thr Leu Gly Gly Thr Leu Thr Ile Thr  
 85 90 95  
 Leu Arg Asn Leu Gln Pro His Asp Ala Gly Leu Tyr Gln Cys Gln Ser  
 20 100 105 110  
 Leu His Gly Ser Glu Ala Asp Thr Leu Arg Lys Val Leu Val Glu Val  
 115 120 125  
 25 Leu Ala Asp Pro Leu Asp His Arg Asp Ala Gly Asp Leu Trp Phe Pro  
 130 135 140  
 Gly Glu Ser Glu Ser Phe Glu Asp Ala His Val Glu His Ser Ile Ser  
 145 150 155 160  
 30 Arg Ser Leu Leu Glu Gly Glu Ile Pro Phe Pro Pro Thr Ser Ile Leu  
 165 170 175  
 Leu Leu Leu Ala Cys Ile Phe Leu Ile Lys Ile Leu Ala Ala Ser Xaa  
 35 180 185 190  
 Leu Trp Ala Ala Ala Trp His Gly Gln Lys Pro Gly Thr His Pro Pro  
 195 200 205  
 40 Ser Glu Leu Asp Cys Gly His Asp Pro Gly Tyr Gln Leu Gln Thr Leu  
 210 215 220  
 Pro Gly Leu Arg Asp Thr  
 225 230  
 45

(2) INFORMATION FOR SEQ ID NO: 215:

50 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 231 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 215:

Met Glu Pro Leu Arg Leu Leu Ile Leu Leu Phe Val Thr Glu Leu Ser  
 1 5 10 15  
 Gly Ala His Asn Thr Thr Val Phe Gln Gly Val Ala Gly Gln Ser Leu  
 60 20 25 30

330

Gln Val Ser Cys Pro Tyr Asp Ser Met Lys His Trp Gly Arg Arg Lys  
           35                          40                          45  
 5 Ala Trp Cys Arg Gln Leu Gly Glu Lys Gly Pro Cys Gln Arg Val Val  
       50                          55                          60  
 Ser Thr His Asn Leu Trp Leu Leu Ser Phe Leu Arg Arg Trp Asn Gly  
   65                          70                          75                          80  
 10 Ser Thr Ala Ile Thr Asp Asp Thr Leu Gly Gly Thr Leu Thr Ile Thr  
                           85                          90                          95  
 Leu Arg Asn Leu Gln Pro His Asp Ala Gly Leu Tyr Gln Cys Gln Ser  
 15                          100                          105                          110  
 Leu His Gly Ser Glu Ala Asp Thr Leu Arg Lys Val Leu Val Glu Val  
       115                          120                          125  
 20 Leu Ala Asp Pro Leu Asp His Arg Asp Ala Gly Asp Leu Trp Phe Pro  
       130                          135                          140  
 Gly Glu Ser Glu Ser Phe Glu Asp Ala His Val Glu His Ser Ile Ser  
   145                          150                          155                          160  
 25 Arg Ser Leu Leu Glu Gly Glu Ile Pro Phe Pro Pro Thr Ser Ile Leu  
                           165                          170                          175  
 Leu Leu Leu Ala Cys Ile Phe Leu Ile Lys Ile Leu Ala Ala Ser Ala  
 30                          180                          185                          190  
 Leu Trp Ala Ala Ala Trp His Gly Gln Lys Pro Gly Thr His Pro Pro  
       195                          200                          205  
 35 Ser Glu Leu Asp Cys Gly His Asp Pro Gly Tyr Gln Leu Gln Thr Leu  
       210                          215                          220  
 Pro Gly Leu Arg Asp Thr Xaa  
   225                          230  
 40

(2) INFORMATION FOR SEQ ID NO: 216:

45 (i) SEQUENCE CHARACTERISTICS:  
       (A) LENGTH: 127 amino acids  
       (B) TYPE: amino acid  
       (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 216:  
 50 Met Gly Leu Thr Gly Phe Gly Val Phe Phe Leu Phe Phe Gly Met Ile  
       1                          5                          10                          15  
 Leu Phe Phe Asp Lys Ala Leu Leu Ala Ile Gly Asn Val Leu Phe Val  
 55                          20                          25                          30  
 Ala Gly Leu Ala Phe Val Ile Gly Leu Glu Arg Thr Phe Arg Phe Phe  
       35                          40                          45  
 60 Phe Gln Lys His Lys Met Lys Ala Thr Gly Phe Phe Leu Gly Gly Val



331

50                                      55                                      60

Phe Val Val Leu Ile Gly Trp Pro Leu Ile Gly Met Ile Phe Glu Ile  
 65                                      70                                      75                                      80

5 Tyr Gly Phe Phe Leu Leu Phe Arg Gly Phe Phe Pro Val Val Val Gly  
                                     85                                      90                                      95

10 Phe Ile Arg Arg Val Pro Val Leu Gly Ser Leu Leu Asn Leu Pro Gly  
                                     100                                      105                                      110

Ile Arg Ser Phe Val Asp Lys Val Gly Glu Ser Asn Asn Met Val  
                                     115                                      120                                      125

15

(2) INFORMATION FOR SEQ ID NO: 217:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 47 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 217:

25 Met Ile Arg Lys Leu His Lys Ile Ile Val Phe Ser Pro Arg Val Ile  
                                     1                                      5                                      10                                      15

Val Leu Leu Asn Cys Phe Phe Phe Ile Lys Ala Lys Phe Val Leu Tyr  
                                     20                                      25                                      30

30 Ile Phe Val Phe His Val Leu Asp Gly Ser Ile Ser Tyr Pro Val  
                                     35                                      40                                      45

35

(2) INFORMATION FOR SEQ ID NO: 218:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 41 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 218:

45 Met Leu Leu Asn Gln His Phe Lys Ile Phe Gly Ser Leu Ile His Met  
                                     1                                      5                                      10                                      15

Asn Leu Leu Phe Ala Leu Ile Ser Leu Gly Ser Ser Asn Leu Ser Gly  
                                     20                                      25                                      30

50 Val Gln Phe Cys Cys Glu Thr Val Gln  
                                     35                                      40

55 (2) INFORMATION FOR SEQ ID NO: 219:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 105 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

60

332

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 219:

5 Met Gln Pro Leu Asn Phe Ser Ser Thr Xaa Cys Ser Ser Phe Ser Pro  
 1 5 10 15  
 Pro Thr Thr Val Ile Leu Leu Ile Leu Leu Cys Phe Glu Gly Leu Leu  
 20 25 30  
 10 Phe Leu Ile Phe Thr Ser Val Met Phe Gly Thr Gln Val His Ser Ile  
 35 40 45  
 Cys Thr Asp Glu Thr Gly Ile Glu Gln Leu Lys Lys Glu Glu Arg Arg  
 50 55 60  
 15 Trp Ala Lys Lys Thr Lys Trp Met Asn Met Lys Ala Val Phe Gly His  
 65 70 75 80  
 Pro Phe Ser Leu Gly Trp Ala Ser Pro Phe Ala Thr Pro Asp Gln Gly  
 85 90 95  
 20 Lys Ala Asp Pro Tyr Gln Tyr Val Val  
 100 105

25

(2) INFORMATION FOR SEQ ID NO: 220:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 29 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 220:

35 Met Tyr Thr Asn His Phe Asn Leu Tyr Leu Lys Tyr Ile Leu Leu Ile  
 1 5 10 15  
 Ile Leu Ile Leu Asn Met Thr Asn Ser Ser Ser Arg Tyr  
 20 25

40

(2) INFORMATION FOR SEQ ID NO: 221:

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 17 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 221:

50 Met Asn Glu Leu Leu Leu Phe Phe Phe Phe Phe Phe Phe Leu His Phe  
 1 5 10 15  
 Val

55

(2) INFORMATION FOR SEQ ID NO: 222:

60

(i) SEQUENCE CHARACTERISTICS:

333

(A) LENGTH: 138 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 222:

5

Met Lys Phe Thr Thr Leu Leu Phe Leu Ala Ala Val Ala Gly Ala Leu  
 1 5 10 15

10

Val Tyr Ala Glu Asp Ala Ser Ser Asp Ser Thr Gly Ala Asp Pro Ala  
 20 25 30

Gln Glu Ala Gly Thr Ser Lys Pro Asn Glu Glu Ile Ser Gly Pro Ala  
 35 40 45

15

Glu Pro Ala Ser Pro Pro Glu Thr Thr Thr Thr Ala Gln Glu Xaa Ser  
 50 55 60

Ala Ala Ala Val Gln Gly Thr Ala Lys Val Thr Ser Ser Arg Gln Glu  
 65 70 75 80

20

Leu Asn Pro Leu Lys Ser Ile Val Glu Lys Ser Ile Leu Leu Thr Glu  
 85 90 95

25

Gln Ala Leu Ala Lys Ala Gly Lys Gly Met His Gly Gly Val Pro Gly  
 100 105 110

Gly Lys Gln Phe Ile Glu Asn Gly Ser Glu Phe Ala Gln Lys Leu Leu  
 115 120 125

30

Lys Lys Phe Ser Leu Leu Lys Pro Trp Ala  
 130 135

35

(2) INFORMATION FOR SEQ ID NO: 223:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 50 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 223:

Met Leu Gly Cys Gly Ile Pro Ala Leu Gly Leu Leu Leu Leu Gln  
 1 5 10 15

45

Xaa Ser Ala Asp Gly Asn Gly Ile Gln Gly Phe Phe Tyr Pro Trp Ser  
 20 25 30

50

Cys Glu Gly Asp Ile Trp Asp Arg Glu Ser Cys Gly Gly Gln Ala Ala  
 35 40 45

Ile Arg  
 50

55

(2) INFORMATION FOR SEQ ID NO: 224:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

60

334

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 224:

5 Met Glu Ala Val Phe Thr Val Phe Phe Phe Leu Leu Phe Cys Phe  
 1 5 10 15

10 (2) INFORMATION FOR SEQ ID NO: 225:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 155 amino acids

(B) TYPE: amino acid

15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 225:

Met Gly Phe Gly Ala Thr Leu Ala Val Gly Leu Thr Ile Phe Val Leu  
 1 5 10 15

20 Ser Val Val Thr Ile Ile Ile Cys Phe Thr Cys Ser Cys Cys Cys Leu  
 20 25 30

25 Tyr Lys Thr Cys Arg Arg Pro Arg Pro Val Val Thr Thr Thr Ser  
 35 40 45

Thr Thr Val Val His Ala Pro Tyr Pro Gln Pro Pro Ser Val Pro Pro  
 50 55 60

30 Ser Tyr Pro Gly Pro Ser Tyr Gln Gly Tyr His Thr Met Pro Pro Gln  
 65 70 75 80

Pro Gly Met Pro Ala Ala Pro Tyr Pro Met Gln Tyr Pro Pro Pro Tyr  
 85 90 95

35 Pro Ala Gln Pro Met Gly Pro Pro Ala Tyr His Glu Thr Leu Ala Gly  
 100 105 110

40 Gly Ala Ala Ala Pro Tyr Pro Ala Ser Gln Pro Pro Tyr Asn Pro Xaa  
 115 120 125

Tyr Met Asp Ala Pro Lys Xaa Xaa Ser Glu His Ser Leu Ala Ser Leu  
 130 135 140

45 Ala Ala Thr Trp Leu Cys Cys Val Cys Ala Xaa  
 145 150 155

50 (2) INFORMATION FOR SEQ ID NO: 226:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

55 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 226:

Met Gly Phe Gly Ala Thr Leu Ala Val Gly  
 1 5 10

60

## (2) INFORMATION FOR SEQ ID NO: 227:

5

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 227:

10

Met Ser Ile Phe Leu Val Met Ser Ile Ser Cys Ser Ser Thr Ser His  
 1 5 10 15

15

Cys Tyr Ser Phe  
 20

## (2) INFORMATION FOR SEQ ID NO: 228:

20

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 94 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 228:

Met Ser Phe Ser Phe Ile Ile Phe Leu Leu Leu Val Cys Gln Glu Ile  
 1 5 10 15

30

Thr Phe Cys Met Ser Tyr Gly Asp Ala Val Asn Cys Phe Ser Glu Cys  
 20 25 30

Phe Ser Asn Leu Gln Thr Ile Tyr Ile Ser Cys Leu Gln His Ala Val  
 35 40 45

35

Cys Lys His Ser Val Ile Trp Ser Ile Gln Leu Phe Val Arg Ala Leu  
 50 55 60

40

Pro Ile Ser Lys Cys Ala Glu Leu Ser Ile Asp Gly Ile Phe Arg Ser  
 65 70 75 80

Phe His Glu Asn Trp Lys Cys Ser Trp Val Ala Pro Thr Xaa  
 85 90

45

## (2) INFORMATION FOR SEQ ID NO: 229:

50

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 94 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 229:

55

Met Ser Phe Ser Phe Ile Ile Phe Leu Leu Leu Val Cys Gln Glu Ile  
 1 5 10 15

Thr Phe Cys Met Ser Tyr Gly Asp Ala Val Asn Cys Phe Ser Glu Cys  
 20 25 30

60

336

Phe Ser Asn Leu Gln Thr Ile Tyr Ile Ser Cys Leu Gln His Ala Val  
 35 40 45

5 Cys Lys His Ser Val Ile Trp Ser Ile Gln Leu Phe Val Arg Ala Leu  
 50 55 60

Pro Ile Ser Lys Cys Ala Glu Leu Ser Ile Asp Gly Ile Phe Arg Ser  
 65 70 75 80

10 Phe His Glu Asn Trp Lys Cys Ser Trp Val Ala Pro Thr Xaa  
 85 90

15 (2) INFORMATION FOR SEQ ID NO: 230:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 37 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 230:

Met Gly Trp Ser Ala Gly Leu Leu Phe Leu Leu Ile Leu Tyr Leu Pro  
 1 5 10 15

25 Val Pro Gly Trp Met Glu Arg Glu Asp Gly Gly Asp Gly Thr Ser Phe  
 20 25 30

Thr Ser Gly Ser Trp  
 35

30

35 (2) INFORMATION FOR SEQ ID NO: 231:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 81 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 231:

Met Ala Thr Leu Trp Gly Gly Leu Leu Arg Leu Gly Ser Leu Leu Ser  
 1 5 10 15

45 Leu Ser Cys Leu Ala Leu Ser Val Leu Leu Leu Ala His Val Gln Thr  
 20 25 30

Pro Pro Arg Ile Ser Arg Met Ser Asp Val Asn Val Ser Ala Leu Pro  
 35 40 45

50 Ile Lys Lys Ile Leu Gly Ile Phe Ile Ile Arg Thr Tyr Leu Arg Lys  
 50 55 60

Ile Val Ile Ala Phe Met Leu Trp Ser Pro Cys Leu Cys Gly Gly Leu  
 55 65 70 75 80

Met

60

## (2) INFORMATION FOR SEQ ID NO: 232:

## (i) SEQUENCE CHARACTERISTICS:

5

(A) LENGTH: 301 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 232:

10 Met Asp Ala Arg Trp Trp Ala Val Val Val Leu Ala Ala Phe Pro Ser  
     1                    5                    10                    15  
     Leu Gly Ala Gly Gly Glu Thr Pro Glu Ala Pro Pro Glu Ser Trp Thr  
                     20                    25                    30  
 15 Gln Leu Trp Phe Phe Arg Phe Val Val Asn Ala Ala Gly Tyr Ala Xaa  
                     35                    40                    45  
 20 Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Phe Arg Arg Lys Asn  
                     50                    55                    60  
     Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys  
                     65                    70                    75                    80  
 25 Val Phe Gly Asn Glu Pro Lys Ala Ser Asp Glu Val Pro Leu Ala Pro  
                     85                    90                    95  
     Arg Thr Glu Ala Ala Glu Thr Thr Pro Met Trp Gln Ala Leu Lys Leu  
                     100                    105                    110  
 30 Leu Phe Cys Ala Thr Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Val  
                     115                    120                    125  
     Leu Gln Glu Arg Val Met Thr Arg Ser Tyr Gly Ala Thr Ala Thr Ser  
 35                    130                    135                    140  
     Pro Gly Glu Arg Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg  
                     145                    150                    155                    160  
 40 Val Leu Ala Leu Ile Val Ala Gly Leu Ser Cys Val Leu Cys Lys Gln  
                     165                    170                    175  
     Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser  
                     180                    185                    190  
 45 Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser  
                     195                    200                    205  
     Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met  
 50                    210                    215                    220  
     Leu Met Gly Lys Leu Val Ser Arg Arg Xaa Asn Glu His Trp Glu Tyr  
                     225                    230                    235                    240  
 55 Leu Thr Ala Thr Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser  
                     245                    250                    255  
     Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu  
 60                    260                    265                    270

338

Ile Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp  
 275 280 285

5 Gln Asp Ala Cys Leu Pro Ile Arg Cys His Arg Cys Arg  
 290 295 300

10 (2) INFORMATION FOR SEQ ID NO: 233:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 313 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 233:

Met Ser Asp Leu Leu Leu Leu Gly Leu Ile Gly Gly Leu Thr Leu Leu  
 1 5 10 15

20 Leu Leu Leu Thr Leu Leu Ala Phe Ala Gly Tyr Ser Gly Leu Leu Ala  
 20 25 30

Gly Val Glu Val Ser Ala Gly Ser Pro Pro Ile Arg Asn Val Thr Val  
 35 40 45

25 Ala Tyr Lys Phe His Met Gly Leu Tyr Gly Glu Thr Gly Arg Leu Phe  
 50 55 60

30 Thr Glu Ser Cys Ser Ile Ser Pro Lys Leu Arg Ser Ile Ala Val Tyr  
 65 70 75 80

Tyr Asp Asn Pro His Met Val Pro Pro Asp Lys Cys Arg Cys Ala Val  
 85 90 95

35 Gly Ser Ile Leu Ser Glu Gly Glu Glu Ser Pro Ser Pro Glu Leu Ile  
 100 105 110

Asp Leu Tyr Gln Lys Phe Gly Phe Lys Val Phe Ser Phe Pro Ala Pro  
 115 120 125

40 Ser His Val Val Thr Ala Thr Phe Pro Tyr Thr Thr Ile Leu Ser Ile  
 130 135 140

45 Trp Leu Ala Thr Arg Arg Val His Pro Ala Leu Asp Thr Tyr Ile Lys  
 145 150 155 160

Glu Arg Lys Leu Cys Ala Tyr Pro Arg Leu Glu Ile Tyr Gln Glu Asp  
 165 170 175

50 Gln Ile His Phe Met Cys Pro Leu Ala Xaa Gln Gly Asp Phe Tyr Val  
 180 185 190

Pro Glu Met Lys Glu Thr Glu Trp Lys Trp Arg Gly Leu Val Glu Ala  
 195 200 205

55 Ile Asp Thr Gln Val Asp Gly Thr Gly Ala Asp Thr Met Ser Asp Thr  
 210 215 220

60 Ser Ser Val Ser Leu Glu Val Ser Pro Gly Ser Arg Glu Thr Ser Ala  
 225 230 235 240



339

Ala Thr Leu Ser Pro Gly Ala Ser Ser Arg Gly Trp Asp Asp Gly Asp  
 245 250 255

5 Thr Arg Ser Glu His Ser Tyr Ser Glu Ser Gly Ala Ser Gly Ser Ser  
 260 265 270

Phe Glu Glu Leu Asp Leu Glu Gly Glu Gly Pro Leu Gly Glu Ser Arg  
 275 280 285

10 Leu Asp Pro Gly Thr Xaa Pro Leu Gly Thr Thr Lys Trp Leu Trp Glu  
 290 295 300

15 Pro Thr Ala Pro Glu Lys Gly Lys Glu  
 305 310

20 (2) INFORMATION FOR SEQ ID NO: 234:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 48 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 234:

Pro Gln Ser Leu Ile Leu His Leu Leu Leu Phe Phe Phe Leu Leu Phe  
 1 5 10 15

30 Leu Phe Phe Ile Phe Ile Phe Leu Phe Phe Leu Gln Cys Leu Thr Phe  
 20 25 30

Leu Phe Xaa Lys Pro Arg Gly Arg Tyr His Gly Leu Cys Phe Lys Phe  
 35 40 45

35

40

(2) INFORMATION FOR SEQ ID NO: 235:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 amino acids

45 (B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 235:

50 Pro Ala Leu Arg Pro Ala Leu Leu Trp Ala Leu Leu Ala Leu Trp Leu  
 1 5 10 15

Cys Cys Ala Thr Pro Arg Met His Cys Ser Val Glu Met Ala Met Asn  
 20 25 30

55 Pro Val

60 (2) INFORMATION FOR SEQ ID NO: 236:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 313 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 236:

5 Met Thr Arg Gly Gly Pro Gly Gly Arg Pro Gly Leu Pro Gln Pro Pro  
 1 5 10 15  
 10 Pro Leu Leu Leu Leu Leu Leu Xaa Leu Leu Leu Val Thr Ala Glu  
 20 25 30  
 15 Pro Pro Lys Pro Ala Gly Val Tyr Tyr Ala Thr Ala Tyr Trp Met Pro  
 35 40 45  
 Ala Glu Lys Thr Val Gln Val Lys Asn Val Met Asp Lys Asn Gly Asp  
 50 55 60  
 20 Ala Tyr Gly Phe Tyr Asn Asn Ser Val Lys Thr Thr Gly Trp Gly Ile  
 65 70 75 80  
 Leu Glu Ile Arg Ala Gly Tyr Gly Ser Gln Thr Leu Ser Asn Glu Ile  
 85 90 95  
 25 Ile Met Phe Val Ala Gly Phe Leu Glu Gly Tyr Leu Thr Ala Pro His  
 100 105 110  
 30 Met Asn Asp His Tyr Thr Asn Leu Tyr Pro Gln Leu Ile Thr Lys Pro  
 115 120 125  
 Ser Ile Met Asp Lys Val Gln Asp Phe Met Glu Lys Gln Asp Lys Trp  
 130 135 140  
 35 Thr Arg Lys Asn Ile Lys Glu Tyr Lys Thr Asp Ser Phe Trp Arg His  
 145 150 155 160  
 Thr Gly Tyr Val Met Ala Gln Ile Asp Gly Leu Tyr Val Gly Ala Lys  
 165 170 175  
 40 Lys Arg Ala Ile Leu Glu Gly Thr Lys Pro Met Thr Leu Phe Gln Ile  
 180 185 190  
 Gln Phe Leu Asn Ser Val Gly Asp Leu Leu Asp Leu Ile Pro Ser Leu  
 195 200 205  
 45 Ser Pro Thr Lys Asn Gly Ser Leu Lys Val Phe Lys Arg Trp Asp Met  
 210 215 220  
 50 Gly His Cys Ser Ala Leu Ile Lys Val Leu Pro Gly Phe Glu Asn Ile  
 225 230 235 240  
 Leu Phe Ala His Ser Ser Trp Tyr Thr Tyr Ala Ala Met Leu Arg Ile  
 245 250 255  
 55 Tyr Lys His Trp Asp Phe Asn Xaa Ile Asp Lys Asp Thr Ser Ser Ser  
 260 265 270  
 60 Arg Leu Ser Phe Ser Ser Tyr Pro Gly Phe Leu Glu Ser Leu Asp Asp  
 275 280 285

Phe Tyr Ile Leu Ser Ser Gly Leu Ile Leu Leu Gln Thr Thr Asn Ser  
290 295 300

5 Val Phe Asn Lys Thr Leu Leu Lys Gln  
305 310

10 (2) INFORMATION FOR SEQ ID NO: 237:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 296 amino acids

(B) TYPE: amino acid

15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 237:

Met Leu Gln Gly Pro Gly Ser Leu Leu Leu Leu Phe Leu Ala Ser His  
1 5 10 15  
20 Cys Cys Leu Gly Ser Ala Arg Gly Leu Phe Leu Phe Gly Gln Pro Asp  
20 25 30  
25 Phe Ser Tyr Lys Arg Xaa Asn Cys Lys Pro Ile Pro Val Asn Leu Gln  
35 40 45  
Leu Cys His Gly Ile Glu Tyr Gln Asn Met Arg Leu Pro Asn Leu Leu  
50 55 60  
30 Gly His Glu Thr Met Lys Glu Val Leu Glu Gln Ala Gly Ala Trp Ile  
65 70 75 80  
Pro Leu Val Met Lys Gln Cys His Pro Asp Thr Lys Lys Phe Leu Cys  
85 90 95  
35 Ser Leu Phe Ala Pro Val Cys Leu Asp Asp Leu Asp Glu Thr Ile Gln  
100 105 110  
40 Pro Cys His Ser Leu Cys Val Gln Val Lys Asp Arg Cys Ala Pro Val  
115 120 125  
Met Ser Ala Phe Gly Phe Pro Trp Pro Asp Met Leu Glu Cys Asp Arg  
130 135 140  
45 Phe Pro Gln Asp Asn Asp Leu Cys Ile Pro Leu Ala Ser Ser Asp His  
145 150 155 160  
Leu Leu Pro Ala Thr Glu Glu Ala Pro Lys Val Cys Glu Ala Cys Lys  
165 170 175  
50 Asn Lys Asn Asp Asp Asp Asn Asp Ile Met Glu Thr Leu Cys Lys Asn  
180 185 190  
55 Asp Phe Ala Leu Lys Ile Lys Val Lys Glu Ile Thr Tyr Ile Asn Arg  
195 200 205  
Asp Thr Lys Ile Ile Leu Glu Thr Lys Ser Lys Thr Ile Tyr Lys Leu  
210 215 220  
60 Asn Gly Val Ser Glu Arg Asp Leu Lys Lys Ser Val Leu Trp Leu Lys

342

	225				230					235				240
	Asp	Ser	Leu	Gln	Cys	Thr	Cys	Glu	Glu	Met	Asn	Asp	Ile	Asn
					245					250				255
5														
	Tyr	Leu	Val	Met	Gly	Gln	Lys	Gln	Gly	Gly	Glu	Leu	Val	Ile
				260						265				270
10														
	Val	Lys	Arg	Trp	Gln	Lys	Gly	Gln	Arg	Glu	Phe	Lys	Arg	Ile
				275					280					285
	Ser	Ile	Arg	Lys	Leu	Gln	Cys	Xaa						
							290	295						

15

(2) INFORMATION FOR SEQ ID NO: 238:

20 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 92 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear  
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 238:

25	Met	Ala	Ser	Leu	Gly	His	Ile	Leu	Val	Phe	Cys	Val	Gly	Leu	Leu	Thr
	1				5					10					15	
	Met	Ala	Lys	Ala	Glu	Ser	Pro	Lys	Glu	His	Asp	Pro	Phe	Thr	Tyr	Asp
				20					25					30		
30	Tyr	Gln	Ser	Leu	Gln	Ile	Gly	Gly	Leu	Val	Ile	Ala	Gly	Ile	Leu	Phe
			35					40					45			
	Ile	Leu	Gly	Ile	Leu	Ile	Val	Leu	Ser	Arg	Arg	Cys	Arg	Cys	Lys	Phe
35		50					55					60				
	Asn	Gln	Gln	Gln	Arg	Thr	Gly	Glu	Pro	Asp	Glu	Glu	Glu	Gly	Thr	Phe
	65					70					75					80
40	Arg	Ser	Ser	Ile	Arg	Arg	Leu	Ser	Xaa	Arg	Xaa	Arg				
					85					90						

45 (2) INFORMATION FOR SEQ ID NO: 239:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 71 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 239:

Met Pro Gly Thr Phe Leu Arg Pro Phe Val Phe Leu Phe Leu Phe Ile  
1 5 10 15

Cys Cys Cys Leu His Ser Gly Gly Leu Gly Gly Val Pro Leu Pro Pro  
20 25 30

Phe Pro Pro Gln Ala Gln Arg Gly Glu Gly Pro Gly Lys Trp Met Ser  
35 40 45

343

Pro Pro Leu Pro Pro His Pro Val Val Ala Pro Pro Thr Pro Ser Pro  
 50 55 60

5 Ser Arg Gly Cys Val Leu Leu  
 65 70

10 (2) INFORMATION FOR SEQ ID NO: 240:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 71 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 240:

Met Pro Gly Thr Phe Leu Arg Pro Phe Val Phe Leu Phe Leu Phe Ile  
 1 5 10 15

20

Cys Cys Cys Leu His Ser Gly Gly Leu Gly Gly Val Pro Leu Pro Pro  
 20 25 30

25

Phe Pro Pro Gln Ala Gln Arg Gly Glu Gly Pro Gly Lys Trp Met Ser  
 35 40 45

Pro Pro Leu Pro Pro His Pro Val Val Ala Pro Pro Thr Pro Ser Pro  
 50 55 60

30

Ser Arg Gly Cys Val Leu Leu  
 65 70

35 (2) INFORMATION FOR SEQ ID NO: 241:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 28 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 241:

Met Phe Tyr Val Leu Ser Val Ser Xaa Leu Xaa Leu Phe Leu Ala Cys  
 1 5 10 15

45

Gly Leu Cys Leu Xaa Leu Leu Thr Gly Lys Leu Leu  
 20 25

50

(2) INFORMATION FOR SEQ ID NO: 242:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 58 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 242:

Met Lys Leu Phe Asp Ala Ser Pro Thr Phe Phe Ala Phe Leu Leu Gly  
 1 5 10 15

60

344

His Ile Leu Ala Met Glu Val Leu Ala Trp Leu Leu Ile Tyr Leu Leu  
                             20                            25                            30

5 Gly Pro Gly Trp Val Pro Ser Ala Leu Xaa Arg Leu His Pro Gly His  
                             35                            40                            45

Leu Ser Gly Ser Val Leu Val Ser Ala Ala  
                             50                            55

10

(2) INFORMATION FOR SEQ ID NO: 243:

15 (i) SEQUENCE CHARACTERISTICS:  
                             (A) LENGTH: 123 amino acids  
                             (B) TYPE: amino acid  
                             (D) TOPOLOGY: linear  
                             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 243:

20 Met Ile Leu Gly Gly Ile Val Val Val Leu Val Phe Thr Gly Phe Val  
                             1                            5                            10                            15

25 Trp Ala Ala His Asn Lys Asp Val Leu Arg Arg Met Lys Lys Arg Tyr  
                             20                            25                            30

Pro Thr Thr Phe Val Met Val Val Met Leu Ala Ser Tyr Phe Leu Ile  
                             35                            40                            45

30 Ser Met Phe Gly Gly Val Met Val Phe Val Phe Gly Ile Thr Phe Pro  
                             50                            55                            60

Leu Leu Leu Met Phe Ile His Ala Ser Leu Arg Leu Arg Asn Leu Lys  
                             65                            70                            75                            80

35 Asn Lys Leu Glu Asn Lys Met Glu Gly Ile Gly Leu Lys Arg Thr Pro  
                             85                            90                            95

40 Met Gly Ile Val Leu Asp Ala Leu Glu Gln Gln Glu Glu Gly Ile Asn  
                             100                            105                            110

Arg Leu Thr Asp Tyr Ile Ser Lys Val Lys Glu  
                             115                            120

45

(2) INFORMATION FOR SEQ ID NO: 244:

50 (i) SEQUENCE CHARACTERISTICS:  
                             (A) LENGTH: 73 amino acids  
                             (B) TYPE: amino acid  
                             (D) TOPOLOGY: linear  
                             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 244:

55 Ala Leu Val Ser Gly Gln Leu Cys Met Glu Ile Ala Arg Gly Asn Ile  
                             1                            5                            10                            15

Phe Phe Leu Asn Xaa Leu Val Thr Thr Phe Cys Cys Ser Cys Leu Leu  
                             20                            25                            30

60

345

Leu Ser Val Xaa Tyr Leu His Xaa Gly Phe Phe Tyr Ser Ser Leu Cys  
                   35                  40                  45  
 5 Lys Cys Cys Phe Val Leu Val Val Leu Ser Arg Ile Gly Ser Val Asn  
                   50                  55                  60  
 Glu Thr Trp Ser Cys Asn Phe Ser Ile  
                   65                  70

10

(2) INFORMATION FOR SEQ ID NO: 245:

(i) SEQUENCE CHARACTERISTICS:  
 15 (A) LENGTH: 49 amino acids  
      (B) TYPE: amino acid  
      (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 245:

20 Thr Pro Ala Thr Thr Ser Ser Ser Ser Ser Pro Leu Phe Leu Ser Ser  
      1                  5                  10                  15  
 Pro Asp Trp Ser Ser Cys Pro Ser Gly Ser Cys Ile Ala Pro Trp Cys  
                   20                  25                  30  
 25 Thr His Trp Ser Ser Ile Leu Pro Ser Leu Xaa Ile Thr Ser Ser Ile  
                   35                  40                  45  
 Pro

30

(2) INFORMATION FOR SEQ ID NO: 246:

35 (i) SEQUENCE CHARACTERISTICS:  
      (A) LENGTH: 339 amino acids  
      (B) TYPE: amino acid  
      (D) TOPOLOGY: linear  
 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 246:

Met Ala Arg Val Pro Pro Leu Ser Ser Ser Trp Thr Ser Ser Arg Tyr  
      1                  5                  10                  15  
 45 Arg Arg Trp Leu Cys Cys Pro Val Trp Trp Thr Thr Phe Trp Ala Thr  
                   20                  25                  30  
 Ala Trp Ser Leu Thr Lys His Leu Tyr Lys Asp Val Thr Asp Ala Ile  
                   35                  40                  45  
 50 Arg Asp Val His Val Lys Gly Leu Met Tyr Gln Trp Ile Glu Gln Asp  
                   50                  55                  60  
 55 Met Glu Lys Tyr Ile Leu Arg Gly Asp Glu Thr Phe Ala Val Leu Ser  
                   65                  70                  75                  80  
 Arg Leu Val Ala His Gly Lys Gln Leu Phe Leu Ile Thr Asn Ser Pro  
                   85                  90                  95  
 60 Phe Ser Phe Val Asp Lys Gly Met Arg His Met Val Gly Pro Asp Trp

346

100 105 110  
 Arg His Ser Ser Met Trp Ser Leu Ser Arg Gln Thr Ser Pro Ala Ser  
 115 120 125  
 5 Ser Leu Thr Gly Ala Thr Phe Arg Lys Leu Asp Glu Lys Gly Ser Leu  
 130 135 140  
 10 Gln Trp Asp Arg Ile Thr Arg Leu Glu Lys Gly Lys Ile Tyr Arg Gln  
 145 150 155 160  
 Gly Asn Leu Phe Asp Phe Leu Arg Leu Thr Glu Trp Arg Gly Pro Arg  
 165 170 175  
 15 Val Leu Tyr Phe Gly Asp His Leu Tyr Ser Asp Leu Ala Asp Leu Met  
 180 185 190  
 Leu Arg His Gly Trp Arg Thr Gly Ala Ile Ile Pro Glu Leu Glu Arg  
 195 200 205  
 20 Glu Ile Arg Ile Ile Asn Thr Glu Gln Tyr Met His Ser Leu Thr Trp  
 210 215 220  
 25 Gln Gln Ala Leu Thr Gly Leu Leu Glu Arg Met Gln Thr Tyr Gln Asp  
 225 230 235 240  
 Ala Glu Ser Arg Gln Val Leu Ala Ala Trp Met Lys Glu Arg Gln Glu  
 245 250 255  
 30 Leu Arg Cys Ile Thr Lys Ala Leu Phe Asn Ala Gln Phe Gly Ser Ile  
 260 265 270  
 Phe Arg Thr Phe His Asn Pro Thr Tyr Phe Ser Arg Arg Leu Val Arg  
 275 280 285  
 35 Phe Ser Asp Leu Tyr Met Ala Ser Leu Ser Cys Leu Leu Asn Tyr Arg  
 290 295 300  
 40 Val Asp Phe Thr Phe Tyr Pro Arg Arg Thr Pro Leu Gln His Glu Ala  
 305 310 315 320  
 Pro Leu Trp Met Asp Gln Leu Leu His Arg Leu His Glu Asp Pro Leu  
 325 330 335  
 45 Pro Trp Xaa

50 (2) INFORMATION FOR SEQ ID NO: 247:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 247:

Met Ala Leu Leu Ser Cys Val Val Asp Tyr Phe Leu Gly His Ser Leu  
 1 5 10 15

60



Xaa Val

5

(2) INFORMATION FOR SEQ ID NO: 248:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 339 amino acids

10

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 248:

15

Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu  
 1 5 10 15

Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu  
 20 25 30

20

Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu  
 35 40 45

Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu  
 50 55 60

25

Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser  
 65 70 75 80

30

Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu  
 85 90 95

Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu  
 100 105 110

35

Thr Asp Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu  
 115 120 125

Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg  
 130 135 140

40

Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu  
 145 150 155 160

45

Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His  
 165 170 175

Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu  
 180 185 190

50

Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His  
 195 200 205

Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr  
 210 215 220

55

Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly pro Val Gln Ser Asn  
 225 230 235 240

60

Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn  
 245 250 255

348

Asn Gly Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu  
 260 265 270

5 Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu  
 275 280 285

Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp  
 290 295 300

10 Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe  
 305 310 315 320

Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr  
 15 325 330 335

Lys His Asp

20

(2) INFORMATION FOR SEQ ID NO: 249:

(i) SEQUENCE CHARACTERISTICS:  
 25 (A) LENGTH: 96 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 249:

30 Met Gly Ala Arg Pro Gly Gly His Pro Gln Lys Trp Ser Phe Leu Trp  
 1 5 10 15

Ser Leu Ala Leu Trp Leu Pro Leu Ala Leu Ser Val Ser Leu Phe Leu  
 20 25 30

35 Gly Leu Ser Leu Ser Pro Pro Gln Pro Gly Leu Ser Leu Trp Cys Thr  
 35 40 45

40 Leu Ser Tyr Cys Cys Glu Gln Trp Lys Phe Lys Gly Thr Pro Ser Pro  
 50 55 60

Ala Leu Leu Asn Leu Gly Thr Gln Pro Lys Lys Asp Lys Lys Leu Glu  
 65 70 75 80

45 Asp Ser Ile Ala Thr Gln Leu Arg Xaa Leu Pro Glu Lys Asn Ser Asn  
 85 90 95

50

(2) INFORMATION FOR SEQ ID NO: 250:

(i) SEQUENCE CHARACTERISTICS:  
 55 (A) LENGTH: 79 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 250:

60

349

Met Ala Leu Thr Phe Leu Leu Val Leu Leu Thr Leu Ala Thr Leu Cys  
 1 5 10 15  
 Thr Arg Leu His Arg Asn Phe Arg Arg Gly Glu Ser Ile Tyr Trp Gly  
 5 20 25 30  
 Pro Thr Ala Asp Ser Gln Asp Thr Val Ala Ala Val Leu Lys Arg Arg  
 35 40 45  
 10 Leu Leu Gln Pro Ser Arg Arg Val Lys Arg Ser Arg Arg Arg Pro Xaa  
 50 55 60  
 Xaa Pro Pro Thr Pro Asp Ser Gly Pro Glu Gly Glu Ser Ser Glu  
 65 70 75  
 15  
 (2) INFORMATION FOR SEQ ID NO: 251:  
 20 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 354 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 251:  
 25 Met Gly Pro Ser Thr Pro Leu Leu Ile Leu Phe Leu Leu Ser Trp Ser  
 1 5 10 15  
 Gly Pro Leu Gln Gly Gln Gln His His Leu Val Glu Tyr Met Glu Arg  
 30 20 25 30  
 Arg Leu Ala Ala Leu Glu Glu Arg Leu Ala Gln Cys Gln Asp Gln Ser  
 35 35 40 45  
 Ser Arg His Ala Ala Glu Leu Arg Asp Phe Lys Asn Lys Met Leu Pro  
 50 55 60  
 Leu Leu Glu Val Ala Glu Lys Glu Arg Glu Ala Leu Arg Thr Glu Ala  
 65 70 75 80  
 40 Asp Thr Ile Ser Gly Arg Val Asp Arg Leu Glu Arg Glu Val Asp Tyr  
 85 90 95  
 Leu Glu Thr Gln Asn Pro Ala Leu Pro Cys Val Glu Phe Asp Glu Lys  
 45 100 105 110  
 Val Thr Gly Gly Pro Gly Thr Lys Gly Lys Gly Arg Arg Asn Glu Lys  
 115 120 125  
 50 Tyr Asp Met Val Thr Asp Cys Gly Tyr Thr Ile Ser Gln Val Arg Ser  
 130 135 140  
 Met Lys Ile Leu Lys Arg Phe Gly Gly Pro Ala Gly Leu Trp Thr Lys  
 145 150 155 160  
 55 Asp Pro Leu Gly Gln Thr Glu Lys Ile Tyr Val Leu Asp Gly Thr Gln  
 165 170 175  
 Asn Asp Thr Ala Phe Val Phe Pro Arg Leu Arg Asp Phe Thr Leu Ala  
 60 180 185 190

350

Met Ala Ala Arg Lys Ala Ser Arg Val Arg Val Pro Phe Pro Trp Val  
 195 200 205

5 Gly Thr Gly Gln Leu Val Tyr Gly Gly Phe Leu Tyr Phe Ala Arg Arg  
 210 215 220

Pro Pro Gly Arg Pro Gly Gly Gly Gly Glu Met Glu Asn Thr Leu Gln  
 225 230 235 240

10 Leu Ile Lys Phe His Leu Ala Asn Arg Thr Val Val Asp Ser Ser Val  
 245 250 255

Phe Pro Ala Glu Gly Leu Ile Pro Pro Tyr Gly Leu Thr Ala Asp Thr  
 15 260 265 270

Tyr Ile Asp Leu Ala Ala Asp Glu Glu Gly Leu Trp Ala Val Tyr Ala  
 275 280 285

20 Thr Arg Glu Asp Asp Arg His Leu Cys Leu Ala Lys Leu Asp Pro Gln  
 290 295 300

Thr Leu Asp Thr Glu Gln Gln Trp Asp Thr Pro Cys Pro Arg Glu Asn  
 305 310 315 320

25 Ala Glu Ala Ala Phe Xaa Ile Cys Gly Thr Leu Tyr Val Val Tyr Asn  
 325 330 335

Thr Arg Pro Ala Ser Arg Ala Arg Ile Gln Cys Ser Phe Asp Ala Ser  
 30 340 345 350

Gly Pro

35

(2) INFORMATION FOR SEQ ID NO: 252:

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 109 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 252:

45 Met Leu Cys Ile Asn Gly Thr Thr Pro Arg Pro Leu Pro Val Pro Ser  
 1 5 10 15

Pro Phe Gly Cys Met Ile Phe Phe Phe Phe Lys Asn Pro Trp Lys Gln  
 20 25 30

50 Arg Leu Leu Gln Gly Trp Leu Gly Ala Arg Pro Ile His Leu Leu Gly  
 35 40 45

Tyr Leu Pro Leu Ser Leu Leu Trp Cys Pro Phe Pro Leu Pro Cys Ala  
 50 55 60

Arg Cys Ser Val Val Tyr Ile Ser Ser Pro Arg His Gly Ala His Ala  
 65 70 75 80

60 Pro Arg Asp Met Ile Leu Ser Leu Val Leu Ala His Gly Ala Leu Tyr

351

85

90

95

Lys Glu Leu Gly Gly Arg Gly Arg Lys Trp Glu Pro Ser  
 100 105

5

(2) INFORMATION FOR SEQ ID NO: 253:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 45 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 253:

15

Met Phe Tyr Phe Leu Pro Leu Ile Phe Pro Ala Phe Pro Pro Trp Ala  
 1 5 10 15

20

Phe Arg Leu Ser Thr Leu Phe Thr Ile Ile Ser Trp Ser Glu Asp Ser  
 20 25 30

Asn Asn Ser Gln Val Tyr Met Asn Cys Val Cys Ser Phe  
 35 40 45

25

(2) INFORMATION FOR SEQ ID NO: 254:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 315 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 254:

35

Met Ala Gly Gly Arg Cys Gly Pro Xaa Leu Thr Ala Leu Leu Ala Ala  
 1 5 10 15

Trp Ile Ala Ala Val Ala Ala Thr Ala Gly Pro Glu Glu Ala Ala Leu  
 20 25 30

40

Pro Pro Glu Gln Ser Arg Val Gln Pro Met Thr Ala Ser Asn Trp Thr  
 35 40 45

45

Leu Val Met Glu Gly Glu Trp Met Leu Lys Phe Tyr Ala Pro Trp Cys  
 50 55 60

Pro Ser Cys Gln Gln Thr Asp Ser Glu Trp Glu Ala Phe Ala Lys Asn  
 65 70 75 80

50

Gly Glu Ile Leu Gln Ile Ser Val Gly Lys Val Asp Val Ile Gln Glu  
 85 90 95

Pro Gly Leu Ser Gly Arg Phe Phe Val Thr Thr Leu Pro Ala Phe Phe  
 100 105 110

55

His Ala Lys Asp Gly Ile Phe Arg Arg Tyr Arg Gly Pro Gly Ile Phe  
 115 120 125

60

Glu Asp Leu Gln Asn Tyr Ile Leu Glu Lys Lys Trp Gln Ser Val Glu  
 130 135 140

352

Pro Leu Thr Gly Trp Lys Ser Pro Ala Ser Leu Thr Met Ser Gly Met  
 145 150 155 160

5 Ala Gly Leu Phe Ser Ile Ser Gly Lys Ile Trp His Leu His Asn Tyr  
 165 170 175

Phe Thr Val Thr Leu Gly Ile Pro Ala Trp Cys Ser Tyr Val Phe Phe  
 180 185 190

10 Val Ile Ala Thr Leu Val Phe Gly Leu Phe Met Gly Leu Val Leu Val  
 195 200 205

Val Ile Ser Glu Cys Phe Tyr Val Pro Leu Pro Arg His Leu Ser Glu  
 210 215 220

15 Arg Ser Glu Gln Asn Arg Arg Ser Glu Glu Ala His Arg Ala Glu Gln  
 225 230 235 240

20 Leu Gln Asp Ala Glu Glu Lys Asp Asp Ser Asn Glu Glu Glu Asn  
 245 250 255

Lys Asp Ser Leu Val Asp Asp Glu Glu Glu Lys Glu Asp Leu Gly Asp  
 260 265 270

25 Glu Asp Glu Ala Glu Glu Glu Glu Glu Glu Asp Asn Leu Ala Ala Gly  
 275 280 285

Val Asp Glu Glu Arg Ser Glu Ala Asn Asp Gln Gly Pro Pro Gly Glu  
 290 295 300

30 Asp Gly Val Thr Arg Glu Xaa Ser Arg Ala Xaa  
 305 310 315

35

(2) INFORMATION FOR SEQ ID NO: 255:

- (i) SEQUENCE CHARACTERISTICS:
- 40 (A) LENGTH: 53 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 255:

45 Met Leu Lys Ala Leu Phe Arg Thr Leu Gln Ala Met Leu Leu Gly Val  
 1 5 10 15

Trp Ile Leu Leu Leu Ala Ser Leu Ala Pro Leu Trp Leu Tyr Cys  
 20 25 30

50 Trp Arg Met Phe Pro Thr Lys Gly Lys Arg Asp Gln Lys Glu Met Leu  
 35 40 45

Glu Val Ser Gly Ile  
 55 50

60

(2) INFORMATION FOR SEQ ID NO: 256:

353

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 93 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 256:

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Pro Val Ala  
 1 5 10 15  
 10 Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr.  
 20 25 30  
 Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro  
 35 40 45  
 15 Leu Leu Ala Gly Leu Val Ala Ala Asp Ala Val Ala Ser Leu Leu Ile  
 50 55 60  
 Val Gly Ala Val Phe Leu Cys Ala Arg Pro Arg Arg Ser Pro Ala Gln  
 20 65 70 75 80  
 Asp Gly Lys Val Tyr Ile Asn Met Pro Gly Arg Gly Xaa  
 85 90

25

## (2) INFORMATION FOR SEQ ID NO: 257:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 12 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

## 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 257:

35 Pro Gly His Leu Leu Pro His Lys Trp Glu Asn Cys  
 1 5 10

## 40 (2) INFORMATION FOR SEQ ID NO: 258:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1852 base pairs

(B) TYPE: nucleic acid

## 45 (C) STRANDEDNESS: double

(D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 258:

50 TGGCATCTGT GAGCAGCTGC CAGGCTCCGG CCAGGATCCC TTCCTTCTCC TCATTGGCTG 60  
 ATGGATCCCA AGGGGCTCCT CTCCTGACC TTCGTGCTGT TTCTCTCCCT GGCITTTGGG 120  
 GCAAGCTACG GAACAGGTGG GCGCATGATG AACTGCCCAA AGATTCTCCG GCAGTIGGGA 180  
 55 AGCAAAGTGC TGCTGCUUCT GACATATGAA AGGATAAATA AGAGCATGAA CAAAAGCATC 240  
 CACATGTGCG TCACAATGGC AAAATCACTG GAGAACAGTG TCGAGAACAA AATAGTGTCT 300  
 60 CTTGATCCAT CCGAAGCAGG CCTCCACGT TATCTAGGAG ATCGCTACAA GTTTTATCTG 360

	GAGAATCTCA CCCTGGGGAT ACGGGAAAGC AGGAAGGAGG ATGAGGGATG GTACCTTATG	420
5	ACCCCTGGAGA AAAATGTTTC AGTTCAGCGC TTTTGCCTGC AGTTGAGGCT TTATGAGCAG	480
	GTCTCCACTC CAGAAATTAA AGTTTTAAAC AAGACCCAGG AGAACGGGAC CTGCACCTTG	540
	ATACTGGGCT GCACAGTGGA GAAGGGGGAC CATGTGGCTT ACAGCTGGAG TGAAAAGGCG	600
10	GGCACCACCC CACTGAACCC AGCCAACAGC TCCCACCTCC TGTCCCTCAC CCTCGGCCCC	660
	CAGCATGCTG ACAATATCTA CATCTGCACC GTGAGCAACC CTATCAGCAA CAATTCCCAG	720
15	ACCTTCAGCC CGTGGCCCGG ATGCAGGACA GACCCCTCAG AAACAAAACC ATGGGCAGTG	780
	TATGCTGGGC TGTTAGGGGG TGTCATCATG ATTCTCATCA TGGTGGTAAT ACTACAGTTG	840
	AGAAGAAGAG GTAAAACGAA CCATTACCAG ACAACAGTGG AAAAAAAG CCTTACGATC	900
20	TATGCCCAAG TCCAGAAACC AGGTGACACT CATCATCAGA CTTGGGACTT ATTCTAATCC	960
	AGGATGACCT TATTTTGAAA TCCTTATCTT GACATCTGTG AAGACCTTTA TTCAAATAAA	1020
25	GTCACATTTT GACATTCTGC GAGGGGCTGG AGCCGGGCGG GGGCGATGTG GAGCGCGGGC	1080
	CGCGGCGGGG CTGCCTGGCC GGTGCTGTGT GGGCTGCTGC TGGCGCTGTT AGTGCCGGGC	1140
	GGTGGTGCCG CCAAGACCGG TCGGAGCTC GTGACTGCGG GTCGGTGCTG AAGCTGCTCA	1200
30	ATACGCACCA CCGGTGCGGC TGCACTCGCA CGACATCAA TACGGATCCG GCAGCGGCCA	1260
	GCAATCGGTG ACCGGCGTAG AGGTGCGAGC GACGAATAGC TACTGGCGGA TCCGCGCGG	1320
35	CTCGGAGGGG GGTGCCCGCG CGGGTCCCCG GTGCGCTGCG GGCAGGCGGT GAGGTACAC	1380
	ATGTGCTTAC GGGCAAGAAC CTGCACACGC ACCACTTCCC GTCGCCGCTG TCCAACAACC	1440
	AGGAAGTGAG TGCCAAAGGG GAAGACGGCG AGGGCGACGA CCTGGACCTA TGGACAGTGC	1500
40	GCTGCTCTGC TCTGGACAGC ACTGGGAGCG TGAGGCTGCT GTGGCGCCTT CCAGCATGTG	1560
	GCACCTCTGT GGTTCCTGTC AGTCACGGTA GCAGTATGGA AGCCCCATCC GTGGGCAGCA	1620
45	TGAGGTCCAC GCATGCCAG TGCCAACAG CACAATACGT GGAAGGCCAT GGAAGGCATC	1680
	TTCATCAAGC CTAGTGTGGA GCCCTCTGCA GGTACGATG AACTCTGAGT GTGTGGATGG	1740
	ATGGGTGGAT GGAGGGTGGC AGGTGGGGCG TCTGCAGGC CACTCTTGGC AGAGACTTTG	1800
50	GGTTTGTAGG GGTCTCAAG TGCCTTTGTG ATTAAAGAAT GTTGGTCTAT GA	1852

55 (2) INFORMATION FOR SEQ ID NO: 259:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 371 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

60



## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 259:

5 Met Glu Leu Glu Leu Asp Ala Gly Asp Gln Asp Leu Leu Ala Phe Leu  
 1 5 10 15  
 Leu Glu Glu Ser Gly Asp Leu Gly Thr Ala Pro Asp Glu Ala Val Arg  
 20 25 30  
 10 Ala Pro Leu Asp Trp Ala Leu Pro Leu Ser Glu Val Pro Ser Asp Trp  
 35 40 45  
 Glu Val Asp Asp Leu Leu Cys Ser Leu Leu Ser Pro Pro Ala Ser Leu  
 50 55 60  
 15 Asn Ile Leu Ser Ser Ser Asn Pro Cys Leu Val His His Asp His Thr  
 65 70 75 80  
 Tyr Ser Leu Pro Arg Glu Thr Val Ser Met Asp Leu Glu Ser Glu Ser  
 85 90 95  
 20 Cys Arg Lys Glu Gly Thr Gln Met Thr Pro Gln His Met Glu Glu Leu  
 100 105 110  
 25 Ala Glu Gln Glu Ile Ala Arg Leu Val Leu Thr Asp Glu Glu Lys Ser  
 115 120 125  
 Leu Leu Glu Lys Glu Gly Leu Ile Leu Pro Glu Thr Leu Pro Leu Thr  
 130 135 140  
 30 Lys Thr Glu Glu Gln Ile Leu Lys Arg Val Arg Arg Lys Ile Arg Asn  
 145 150 155 160  
 Lys Arg Ser Ala Gln Glu Ser Arg Arg Lys Lys Lys Val Tyr Val Gly  
 165 170 175  
 35 Gly Leu Glu Ser Arg Val Leu Lys Tyr Thr Ala Gln Asn Met Glu Leu  
 180 185 190  
 40 Gln Asn Lys Val Gln Leu Leu Glu Glu Gln Asn Leu Ser Leu Leu Asp  
 195 200 205  
 Gln Leu Arg Lys Leu Gln Ala Met Val Ile Glu Ile Ser Asn Lys Thr  
 210 215 220  
 45 Ser Ser Ser Ser Thr Cys Ile Leu Val Leu Leu Val Ser Phe Cys Leu  
 225 230 235 240  
 Leu Leu Val Pro Ala Met Tyr Ser Ser Asp Thr Arg Gly Ser Leu Pro  
 245 250 255  
 50 Ala Glu His Gly Val Leu Ser Arg Gln Leu Arg Ala Leu Pro Ser Glu  
 260 265 270  
 55 Asp Pro Tyr Gln Leu Glu Leu Pro Ala Leu Gln Ser Glu Val Pro Lys  
 275 280 285  
 Asp Ser Thr His Gln Trp Leu Asp Gly Ser Asp Cys Val Leu Gln Ala  
 290 295 300  
 60 Pro Gly Asn Thr Ser Cys Leu Leu His Tyr Met Pro Gln Ala Pro Ser

356

305                      310                      315                      320  
 Ala Glu Pro Pro Leu Glu Trp Pro Phe Pro Asp Leu Ser Ser Glu Pro  
                                  325                      330                      335  
 5    Leu Cys Arg Gly Pro Ile Leu Pro Leu Gln Ala Asn Leu Thr Arg Lys  
                                  340                      345                      350  
 10   Gly Gly Trp Leu Pro Thr Gly Ser Pro Ser Val Ile Leu Gln Asp Arg  
                                  355                      360                      365  
   Tyr Ser Gly  
       370

15

(2) INFORMATION FOR SEQ ID NO: 260:

20        (i) SEQUENCE CHARACTERISTICS:  
           (A) LENGTH: 12 amino acids  
           (B) TYPE: amino acid  
           (D) TOPOLOGY: linear  
       (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 260:

25    Cys Arg Cys Ala Ser Gly Phe Thr Gly Glu Asp Cys  
       1                      5                      10

30 (2) INFORMATION FOR SEQ ID NO: 261:

          (i) SEQUENCE CHARACTERISTICS:  
           (A) LENGTH: 12 amino acids  
           (B) TYPE: amino acid  
 35        (D) TOPOLOGY: linear  
       (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 261:

40    Cys Thr Cys Gln Val Gly Phe Thr Gly Lys Glu Cys  
       1                      5                      10

(2) INFORMATION FOR SEQ ID NO: 262:

45        (i) SEQUENCE CHARACTERISTICS:  
           (A) LENGTH: 12 amino acids  
           (B) TYPE: amino acid  
           (D) TOPOLOGY: linear  
       (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 262:

50    Cys Leu Asn Leu Pro Gly Ser Tyr Gln Cys Gln Cys  
       1                      5                      10

55

(2) INFORMATION FOR SEQ ID NO: 263:

          (i) SEQUENCE CHARACTERISTICS:  
           (A) LENGTH: 12 amino acids  
 60        (B) TYPE: amino acid

357

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 263:

5 Cys Lys Cys Leu Thr Gly Phe Thr Gly Gln Lys Cys  
 1 5 10

(2) INFORMATION FOR SEQ ID NO: 264:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 12 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 264:

Cys Gln Cys Leu Gln Gly Phe Thr Gly Gln Tyr Cys  
 1 5 10

20

(2) INFORMATION FOR SEQ ID NO: 265:

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 127 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 265:

30 Gly Leu Ala Cys Trp Leu Ala Gly Val Ile Phe Ile Asp Arg Lys Arg  
 1 5 10 15

Thr Gly Asp Ala Ile Ser Val Met Ser Glu Val Ala Gln Thr Leu Leu  
 20 25 30

35

Thr Gln Asp Val Xaa Val Trp Val Phe Pro Glu Gly Thr Arg Asn His  
 35 40 45

40 Asn Gly Ser Met Leu Pro Phe Lys Arg Gly Ala Phe His Leu Ala Val  
 50 55 60

Gln Ala Gln Val Pro Ile Val Pro Ile Val Met Ser Ser Tyr Gln Asp  
 65 70 75 80

45 Phe Tyr Cys Lys Lys Glu Arg Arg Phe Thr Ser Gly Gln Cys Gln Val  
 85 90 95

Arg Val Leu Pro Pro Val Pro Thr Glu Gly Leu Thr Pro Asp Asp Val  
 100 105 110

50

Pro Ala Leu Ala Asp Arg Val Arg His Ser Met Leu His Cys Phe  
 115 120 125

55

(2) INFORMATION FOR SEQ ID NO: 266:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 98 amino acids

(B) TYPE: amino acid

60

358

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 266:

5      Pro Ser Ala Lys Tyr Phe Phe Lys Met Ala Phe Tyr Asn Gly Trp Ile  
       1                                5                                10                                15  
       Leu Phe Leu Ala Val Leu Ala Ile Pro Val Cys Ala Val Arg Gly Arg  
                               20                                25                                30  
 10     Asn Val Glu Asn Met Lys Ile Leu Arg Leu Met Leu Leu His Ile Lys  
                               35                                40                                45  
       Tyr Leu Tyr Gly Ile Arg Val Glu Val Arg Gly Ala His His Phe Pro  
                               50                                55                                60  
 15     Pro Ser Gln Pro Tyr Val Val Val Ser Asn His Gln Ser Ser Leu Asp  
                               65                                70                                75                                80  
       Leu Leu Gly Met Met Glu Val Leu Pro Gly Arg Cys Val Pro Ile Ala  
 20                                85                                90                                95  
       Lys Arg

25

(2) INFORMATION FOR SEQ ID NO: 267:

30            (i) SEQUENCE CHARACTERISTICS:  
               (A) LENGTH: 9 amino acids  
               (B) TYPE: amino acid  
               (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 267:

35     Thr Val Phe Arg Glu Ile Ser Thr Asp  
       1                                5

40 (2) INFORMATION FOR SEQ ID NO: 268:

45            (i) SEQUENCE CHARACTERISTICS:  
               (A) LENGTH: 11 amino acids  
               (B) TYPE: amino acid  
               (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 268:

50     Leu Trp Ala Gly Ser Ala Gly Trp Pro Ala Gly  
       1                                5                                10

(2) INFORMATION FOR SEQ ID NO: 269:

55            (i) SEQUENCE CHARACTERISTICS:  
               (A) LENGTH: 29 amino acids  
               (B) TYPE: amino acid  
               (D) TOPOLOGY: linear

60            (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 269:

359

Ser Ile Leu Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala  
 1 5 10 15

5 Ser Lys His Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg  
 20 25

10 (2) INFORMATION FOR SEQ ID NO: 270:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 8 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 270:

Met Ala Tyr His Gly Leu Thr Val  
 1 5

20

(2) INFORMATION FOR SEQ ID NO: 271:

25 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 6 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 271:

30 Ile Ser Ala Ala Arg Val  
 1 5

35 (2) INFORMATION FOR SEQ ID NO: 272:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 11 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 272:

Pro Asp Val Ser Glu Phe Met Thr Arg Leu Phe  
 1 5 10

45

(2) INFORMATION FOR SEQ ID NO: 273:

50 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 17 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 273:

55 Phe Asp Pro Val Arg Val Asp Ile Thr Ser Lys Gly Lys Met Arg Ala  
 1 5 10 15


Arg

360

Applicant's or agent's file reference number	PS001PCT	International application	Unassigned
---	----------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)


A. The indications made below relate to the microorganism referred to in the description on page 64 line N/A	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit February 26, 1997	Accession Number 97901
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application Authorized officer 	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer

361

Applicant's or agent's file reference number	P001PCT	International applicatio.	Unassigned
---	---------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)


A. The indications made below relate to the microorganism referred to in the description on page 64 line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit February 26, 1997	Accession Number 97898
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

Applicant's or agent's file reference number	S001PCT	362	International application	Unassigned
---	---------	-----	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 64 . line N/A	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209044
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<b>For receiving Office use only</b>	<b>For International Bureau use only</b>
<input checked="checked" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer




363

Applicant's or agent's file reference number	P001PCT	International application	Unassigned	1998
---	---------	---------------------------	------------	------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)


A. The indications made below relate to the microorganism referred to in the description on page 64 line N/A	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit February 26, 1997	Accession Number 97899
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application Authorized officer 	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer

364

Applicant's or agent's file reference number	PS001PCT	International applicatio	Unassigned 04482
---	----------	--------------------------	------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)


A. The indications made below relate to the microorganism referred to in the description on page 65 . line N/A	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209045
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application Authorized officer 	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer

Applicant's or agent's file reference number	365 S001PCT	International application	Unassigned
--	----------------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 64 . line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit February 26, 1997	Accession Number 97900
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only
<input checked="" type="checkbox"/> This sheet was received with the international application
Authorized officer 

For International Bureau use only
<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer


366

Applicant's or agent's file reference number	S001PCT	International application	Unassigned
---	---------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 64, line N/A	
B. IDENTIFICATION OF DEPOSIT <span style="float: right;">Further deposits are identified on an additional sheet <input type="checkbox"/></span>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209046
C. ADDITIONAL INDICATIONS (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	


For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer: 	Authorized officer

367

Applicant's or agent's file reference number	S001PCT	International applicant	Unassigned	4482
---	---------	-------------------------	------------	------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)


A. The indications made below relate to the microorganism referred to in the description on page 65, line N/A	
B. IDENTIFICATION OF DEPOSIT	
Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit April 28, 1997	Accession Number 209010
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

368

Applicant's or agent's file reference number	S001PCT	International application	Unassigned	14482
---	---------	---------------------------	------------	-------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 65 line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 29, 1997	Accession Number 209085
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (If the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer


369

Applicant's or agent's file reference number	S001PCT	International application	Unassigned
--	---------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 65 . line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit February 26, 1997	Accession Number 97897
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	


For receiving Office use only	For International Bureau use only
<input checked="checked" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

370

Applicant's or agent's file reference number	PS001PCT	International applicatio	Unassigned
---	----------	--------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)


A. The indications made below relate to the microorganism referred to in the description on page 65 line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209043
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer



Applicant's or agent's file reference number	S001PCT	371	International application	Unassigned
---	---------	-----	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

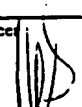
A. The indications made below relate to the microorganism referred to in the description on page 73, line N/A	
B. IDENTIFICATION OF DEPOSIT	
Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit September 4, 1997	Accession Number 209236
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

372

Applicant's or agent's file reference number	S001PCT	International application	Unassigned	12483
---	---------	---------------------------	------------	-------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 73 . line N/A	
B. IDENTIFICATION OF DEPOSIT <span style="float: right;">Further deposits are identified on an additional sheet <input type="checkbox"/></span>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 29, 1997	Accession Number 209084
C. ADDITIONAL INDICATIONS (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

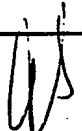
373

Applicant's or agent's file reference number	S001PCT	International application	Unassigned
--	---------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 76 . line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209048
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (If the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input checked="checked" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer


374

Applicant's or agent's file reference number	S001PCT	International application	Unassigned
---	---------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>76</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit February 26, 1997	Accession Number 97902
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	


For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

Applicant's or agent's file reference number	S001PCT	375	International applicant	Unassigned	04482
---	---------	-----	-------------------------	------------	-------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>77</u> . line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <p style="text-align: center;">American Type Culture Collection</p>	
Address of depositary institution (including postal code and country) <p>12301 Parklawn Drive Rockville, Maryland 20852 United States of America</p>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97903</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the Indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")     	


<b>For receiving Office use only</b>	<b>For International Bureau use only</b>
<input checked="checked" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

376

Applicant's or agent's file reference number	S001PCT	International application	Unassigned OFFICE
---	---------	---------------------------	----------------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)


A. The indications made below relate to the microorganism referred to in the description on page <u>77</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209049
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

377

Applicant's or agent's file reference number	S001PCT	International application	Unassigned
---	---------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 80, line N/A	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit February 26, 1997	Accession Number 97904
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")          	
<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application Authorized officer 	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer


378

Applicant's or agent's file reference number	S001PCT	International application	Unassigned
---	---------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 80 line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209050
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input checked="checked" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer




379

Applicant's or agent's file reference number	5001PCT	International application	Unassigned	04482
---	---------	---------------------------	------------	-------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>82</u> line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit April 4, 1997	Accession Number 97976
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer


380

Applicant's or agent's file reference number	5001PCT	International applicant	Unassigned
---	---------	-------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page 64, line N/A	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 12301 Parklawn Drive Rockville, Maryland 20852 United States of America	
Date of deposit May 15, 1997	Accession Number 209047
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<b>For receiving Office use only</b> <input checked="" type="checkbox"/> This sheet was received with the international application Authorized officer 	<b>For International Bureau use only</b> <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
---	--

***What Is Claimed Is:***

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group  
5 consisting of:
  - (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
  - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a  
10 polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
  - (c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
  - 15 (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
  - (e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X,  
20 having biological activity;
  - (f) a polynucleotide which is a variant of SEQ ID NO:X;
  - (g) a polynucleotide which is an allelic variant of SEQ ID NO:X;
  - (h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
  - 25 (i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
2. The isolated nucleic acid molecule of claim 1, wherein the  
30 polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.
3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included  
35 in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

5

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

10

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

15

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

20

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.

25

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;

30

(c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

35

(e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(f) a full length protein of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

- (g) a variant of SEQ ID NO:Y;
- (h) an allelic variant of SEQ ID NO:Y; or
- (i) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the secreted form or the  
5 full length protein comprises sequential amino acid deletions from either the C-terminus  
or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of  
claim 11.

10

14. A recombinant host cell that expresses the isolated polypeptide of claim  
11.

15

15. A method of making an isolated polypeptide comprising:  
(a) culturing the recombinant host cell of claim 14 under conditions such that  
said polypeptide is expressed; and  
(b) recovering said polypeptide.

20

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition,  
comprising administering to a mammalian subject a therapeutically effective amount of  
the polypeptide of claim 11 or the polynucleotide of claim 1.

25

18. A method of diagnosing a pathological condition or a susceptibility to a  
pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of  
claim 1; and

30

(b) diagnosing a pathological condition or a susceptibility to a pathological  
condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a  
pathological condition in a subject comprising:

35

(a) determining the presence or amount of expression of the polypeptide of  
claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological  
condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

- 5 (a) contacting the polypeptide of claim 11 with a binding partner; and  
(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

10 22. A method of identifying an activity in a biological assay, wherein the method comprises:

- (a) expressing SEQ ID NO:X in a cell;  
(b) isolating the supernatant;  
(c) detecting an activity in a biological assay; and  
15 (d) identifying the protein in the supernatant having the activity.


23. The product produced by the method of claim 22.

Applicant's or agent's file reference number	PS001PCT	International application	Unassigned
--	----------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>64</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97900</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;">For receiving Office use only</p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <p>Authorized officer </p>	<p style="text-align: center;">For International Bureau use only</p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
--	--

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.



## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file  
reference number

PS001PCT


International application

Unassigned

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>65</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input checked="" type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 15, 1997</u>	Accession Number <u>209043</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<b>For receiving Office use only</b>	<b>For International Bureau use only</b>
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**Page 2****UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file  
reference number

PS001PCT

International application No. Unassigned

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description  
on page 64, line N/A

### B. IDENTIFICATION OF DEPOSIT

Further deposits are identified on an additional sheet ☒

Name of depositary institution American Type Culture Collection

Address of depositary institution (including postal code and country)

12301 Parklawn Drive  
Rockville, Maryland 20852  
United States of America

Date of deposit May 15, 1997

Accession Number 209044

### C. ADDITIONAL INDICATIONS (leave blank if not applicable)

This information is continued on an additional sheet ☐

In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).

### D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)

### E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)

The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")

For receiving Office use only

☒ This sheet was received with the international application

Authorized officer

For International Bureau use only

☐ This sheet was received by the International Bureau on:

Authorized officer

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

Page 2

#### UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

#### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned	PCT 95/04462
--	----------	--	--------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>65</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 15, 1997</u>	Accession Number <u>209045</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>in respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;"><b>For receiving Office use only</b></p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <hr/> <p>Authorized officer </p>	<p style="text-align: center;"><b>For International Bureau use only</b></p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <hr/> <p>Authorized officer</p>
--	---



**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art

Page 2

#### UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

#### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### NETHERLANDS

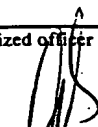
The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned
--	----------	--

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>64</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 15, 1997</u>	Accession Number <u>209046</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	
<input checked="" type="checkbox"/> This sheet was received with the international application	
Authorized officer 	

For International Bureau use only	
<input type="checkbox"/> This sheet was received by the International Bureau on:	
Authorized officer	

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

Page 2

## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file  
reference number

PS001PCT

International application No. Unassigned

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description  
on page 64, line N/A

### B. IDENTIFICATION OF DEPOSIT

Further deposits are identified on an additional sheet ☒

Name of depositary institution American Type Culture Collection

Address of depositary institution (including postal code and country)

12301 Parklawn Drive  
Rockville, Maryland 20852  
United States of America

Date of deposit May 15, 1997

Accession Number 209047

### C. ADDITIONAL INDICATIONS (leave blank if not applicable)

This information is continued on an additional sheet ☐

In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).

### D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)

### E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)

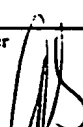
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")

For receiving Office use only



This sheet was received with the international application

Authorized officer



For International Bureau use only



This sheet was received by the International Bureau on:

Authorized officer

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

Page 2

## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.



Applicant's or agent's file reference number	PS001PCT	International application no.	Unassigned
--	----------	-------------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>76</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 15, 1997</u>	Accession Number <u>209048</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;"><b>For receiving Office use only</b></p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <p>Authorized officer </p>	<p style="text-align: center;"><b>For International Bureau use only</b></p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
--	---

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

Page 2

## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application	J. Unassigned
--	----------	---------------------------	---------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>77</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 15, 1997</u>	Accession Number <u>209049</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;"><b>For receiving Office use only</b></p> <div style="border: 1px solid black; padding: 5px;"> <input checked="" type="checkbox"/> This sheet was received with the international application </div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> Authorized officer  </div>	<p style="text-align: center;"><b>For International Bureau use only</b></p> <div style="border: 1px solid black; padding: 5px;"> <input type="checkbox"/> This sheet was received by the International Bureau on: </div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> Authorized officer </div>
--	---

## CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

## NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

Page 2

#### UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

#### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application	Unassigned
--	----------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>80</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 15, 1997</u>	Accession Number <u>209050</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>in respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	
<input checked="" type="checkbox"/> This sheet was received with the international application	
Authorized officer	

For International Bureau use only	
<input type="checkbox"/> This sheet was received by the International Bureau on:	
Authorized officer	

## CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

## NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.



Page 2

#### UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

#### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file  
reference number

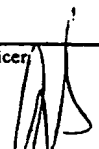
PS001PCT

International application no. unassigned

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>73</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input checked="" type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>September 4, 1997</u>	Accession Number <u>209236</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
in respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	
<input checked="" type="checkbox"/> This sheet was received with the international application	
Authorized officer	

For International Bureau use only	
<input type="checkbox"/> This sheet was received by the International Bureau on:	
Authorized officer	

## CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

## NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned
--	----------	--

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>65</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>April 28, 1997</u>	Accession Number <u>209010</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;"><b>For receiving Office use only</b></p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <p>Authorized officer </p>	<p style="text-align: center;"><b>For International Bureau use only</b></p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
--	---

## CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

## NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**Page 2****UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file  
reference number

PS001PCT


International application

No. Unassigned

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>65</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input checked="" type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 29, 1997</u>	Accession Number <u>209085</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
in respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<b>For receiving Office use only</b>	<b>For International Bureau use only</b>
<input checked="" type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer 	Authorized officer



**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**Page 2****UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file  
reference number

PS001PCT

International application

to: Unassigned

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description  
on page 64, line N/A

### B. IDENTIFICATION OF DEPOSIT

Further deposits are identified on an additional sheet ☒

Name of depositary institution American Type Culture Collection

Address of depositary institution (including postal code and country)

12301 Parklawn Drive  
Rockville, Maryland 20852  
United States of America

Date of deposit February 26, 1997

Accession Number 97901

### C. ADDITIONAL INDICATIONS (leave blank if not applicable)

This information is continued on an additional sheet ☐

in respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).

### D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)

### E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)

The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")

For receiving Office use only



This sheet was received with the international application

Authorized officer



For International Bureau use only



This sheet was received by the International Bureau on:

Authorized officer

## CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

## NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**Page 2****UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned
--	----------	--

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>77</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97903</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (If the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	
<input checked="" type="checkbox"/> This sheet was received with the international application	
Authorized officer	

For International Bureau use only	
<input type="checkbox"/> This sheet was received by the International Bureau on:	
Authorized officer	

## CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

## NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**Page 2****UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by an applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.



Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned
--	----------	--

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>64</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97898</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;">For receiving Office use only</p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <p>Authorized officer </p>	<p style="text-align: center;">For International Bureau use only</p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
---	--

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS


The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned
--	----------	--

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>80</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97904</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;"><b>For receiving Office use only</b></p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <p>Authorized officer </p>	<p style="text-align: center;"><b>For International Bureau use only</b></p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
---	---

## CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

## NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned
--	----------	--

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>73</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>May 29, 1997</u>	Accession Number <u>209084</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	
<input checked="" type="checkbox"/> This sheet was received with the international application	
Authorized officer	

For International Bureau use only	
<input type="checkbox"/> This sheet was received by the International Bureau on:	
Authorized officer	

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.



**Page 2****UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application No. Unassigned
--	----------	--

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>64</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97899</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;"><b>For receiving Office use only</b></p> <div style="border: 1px solid black; padding: 5px;"> <input checked="" type="checkbox"/> This sheet was received with the international application         </div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;">         Authorized officer  </div>	<p style="text-align: center;"><b>For International Bureau use only</b></p> <div style="border: 1px solid black; padding: 5px;"> <input type="checkbox"/> This sheet was received by the International Bureau on:         </div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;">         Authorized officer       </div>
--	---

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art:

Page 2

#### UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

#### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file  
reference number

PS00:PCT

International application No. Unassigned

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>65</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input checked="" type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97897</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (If the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only



This sheet was received with the international application

Authorized officer



For International Bureau use only



This sheet was received by the International Bureau on:

Authorized officer

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

**Page 2****UNITED KINGDOM**

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

**DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

**SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

**NETHERLANDS**

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application	Unassigned
--	----------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>82</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>April 4, 1997</u>	Accession Number <u>97976</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (If the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

For receiving Office use only	
<input checked="" type="checkbox"/> This sheet was received with the international application	
Authorized officer	

For International Bureau use only	
<input type="checkbox"/> This sheet was received by the International Bureau on:	
Authorized officer	



**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

Page 2

## UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

## DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

## SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

**NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

**AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

**FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

Page 2

#### UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

#### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

#### NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PS001PCT	International application	Unassigned
--	----------	---------------------------	------------

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>76</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input checked="" type="checkbox"/></span>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>12301 Parklawn Drive</u> <u>Rockville, Maryland 20852</u> <u>United States of America</u>	
Date of deposit <u>February 26, 1997</u>	Accession Number <u>97902</u>
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<p>In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).</p>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (If the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<p style="text-align: center;"><b>For receiving Office use only</b></p> <p><input checked="" type="checkbox"/> This sheet was received with the international application</p> <p>Authorized officer </p>	<p style="text-align: center;"><b>For International Bureau use only</b></p> <p><input type="checkbox"/> This sheet was received by the International Bureau on:</p> <p>Authorized officer</p>
--	---